THE NATIONAL CLEARINGHOUSE FOR MENTAL HEALTH INFORMATION

VOL 10 NO 12 December 1971

PSYCHOPHARMACOLOGY ABSTRACTS

NATIONAL INSTITUTE OF MENTAL HEALTH

PSYCHOPHARMACOLOGY ABSTRACTS is a publication of the National Clearinghouse for Mental Health Information of the National Institute of Mental Health. It is a specialized information medium designed to assist the Institute in meeting its obligation to foster and support laboratory and clinical research into the nature and causes of mental disorders and methods of treatment and prevention. Specifically, this information service is designed to meet the needs of investigators in the field of psychopharmacology for rapid and comprehensive information about new developments and research results. For information or correspondence with the National Institute of Mental Health concerning *Psychopharmacology Abstracts*, changes of address, or removal of names from the mailing list see the inside back cover page.

Use of funds for printing this publication approved by the Director of the Office of Management and Budget, September 1, 1970.

ABSTRACTS

PRECLINICAL PSYCHOPHARMACOLOGY

01 CHEMICAL SYNTHESIS, ISOLATION AND CHARACTERIZATION

105332 Ketcham, Roger G. University of California, San Francisco Project Summary: Condensed polyheterocycles containing N,S and O. *University of California.* Began September 1, 1967. Completed February 1, 1970.

The reaction of alpha-mercapto acids with cyanogen has been studied and shown to give 2-0(S-carboxyalkyl)-thioimidyl0-delta(2)-thiazolin-4-one in good yields. The reaction product undergoes unusual N-methylation in addition to esterification when treated with diazomethane and could be cyclized to afford bicyclic symmetrical 4,4'-diketo-delta(2)-bithiazolinyl, which could be converted into its dienol diacetate. Proof of structure has been obtained by X-ray crystallography and supporting evidence obtained from UV, IR, NMR, and pKa determinations and dipole moment measurements. A series of functionalized dialkylthiazolothiazoles has been prepared and screened for their somnifacient properties in mice. The conclusions are: 1) these derivatives do not show sufficient activity to be pursued further; 2) the biological activity does not depend on any specific functional group, or even on the presence of functional groups; 3) the slight decrease in activity for higher homologs suggests that low homologs be studied. 23 references. (Author abstract modified)

115027 Keup, Wolfram. Brooklyn State Hospital, NY Structure-activity relationship among hallucinogenic agents. *In: Keup, W., Origin and mechanisms of hallucinations.* New York, Plenum Press, 1970. 479 p. (p.345-376).

The molecular structures of known hallucinogenic substances are reviewed and a tentative chemical classification is offered. Although belonging to different groups, most hallucinogens share a number of distinct characteristics. The structural similarities seem to suggest the existence of a single receptor site for psychotomimetic compounds. Superpositioning of the features of active molecules, as compared to inactive congeners, yields a number of special characteristics of that assumed binding site. A plan is charted as to how such a working hypothesis could be tested. 141 references. (Author abstract)

137993 Matin, Shaikh Badarul. University of California, San Francisco Stereochemical aspects of centrally active compounds. (Ph.D. dissertation). *Dissertation Abstracts International.* Ann Arbor, Mich., Univ. M-films, No. 72-24930 HC$10.00 MF$4.00 156 p.

The stereochemical aspects of centrally active compounds were studied to develop a stereospecific synthesis of naturally occurring 1-methyl-8-hydroxytetrahydroisoquinoline alkaloids and to establish the absolute configuration of certain ring substituted beta-phenylisopropylamines in preparation for comparative metabolic and pharmacologic studies. The investigation was conducted in four parts: 1) an examination of the Fayden-Stevens reaction, which represents a potentially convenient route to aldehyde intermediates needed for the synthesis of tetrahydroisoquinolines; 2) synthesis of 1-methyl-6,7-dimethoxy-8-hydroxy-1,2,3,4-tetrahydroisoquinoline alkaloids; 3) investigation of the stereochemical aspects of hallucinogenic beta-phenylisopropylamines; and 4) investigation of electron capture mechanism and determination of 1 and 2 degree amines in biological fluid using an electron capture detector. (Journal abstract modified)

02 DRUG DEVELOPMENT (PRECLINICAL SCREENING)

114769 Takagi, Hironu; Kamioka, Toshiharu; Kobayshi, Shinsaku; Suzuki, Yoshio; Tachikawa, Ryuju. Research Laboratories Sankyo Co., Tokyo, Japan Pharmacological studies of oxazolazepan, a new psychotropic agent - I.actions on the central nervous system, especially on the behavioral observation. *Annual Report of Sankyo Research Laboratories (Tokyo).* 22:285-286, 1970.

A report on the actions of oxazolazepam, a new psychotropic agent, on the central nervous system is presented, in comparison with that of chlordiazepoxide. Results are based on experiments on mice, hamsters, rats, and monkeys. The results show that oxazolazepam is somewhat more potent against convulsions induced by bemegride and pentylenetetrazol and convulsions of mice. However, it is less potent against convulsions induced by strychnine and electroshock than chlordiazepoxide. Oxazolazepam shows marked taming effects in mice, hamsters, rats and monkeys,

which is comparable to those of chlordiazepoxide. On the decrease of spontaneous locomotor activity, muscular relaxation, ataxia and loss of righting reflex in mice and tolerance of taming effects in hamsters, oxazolazepam is definitely less effective than chlordiazepoxide. On the conditioned avoidance response in rats, emesis produced by apomorphine in dogs and tremorine induced symptoms in mice, oxazolazepam is not significantly inhibitory. (Author abstract modified)

114836 Tanase, Hisao; Hirose, Kouichi; Shimada, Kouichi; Aoki, Kaoru; Suzuki, Yoshio. Research Laboratories Sankyo Co., Ltd., Tokyo, Japan The safety test of L-DOPA -- II, effect of L-DOPA on the development of pre- and postnatal offsprings of experimental animals. *Annual Report of Sankyo Research Laboratories (Tokyo).* 22:165-186, 1970.

A report on the effects of L-Dopa on the development of prenatal and postnatal offspring of experimental animals is presented. The drug was administered to mice for six days between the 7th to 12th day of pregnancy and in rats between the 9th to 14th day of pregnancy. The oral dosages were 600, 300 and 150mg/kg/day in mice and 300 and 150mg/kg/day in rats. The intraperitoneal doses were 200, 100 and 50mg/kg/day in mice and 80 and 40mg/kg/day in rats. The fetuses were removed from the dams on the 18th day of pregnancy in mice and on the 20th day of pregnancy in rats, and some offspring from the orally treated animals were left to deliver naturally. L-Dopa does not reveal any teratogenic effect on mouse and rat embryos. However, the growth is suppressed in fetuses of mice and the lethal effect is shown in rat fetuses of the intraperitoneally injected group. Furthermore, the decrease of parturition and nursing rates is observed only in the 600mg/kg/day treated group of mice. 9 references. (Author abstract modified)

114838 Kobayashi, Shinsaku; Koike, Hiroyuki; Nakayama, Koichi; Hasegawa, Kazuo; Oshima, Takeshi; Nishio, Shintaro; Takagi, Hiromu. Research Laboratories Sankyo Co., Ltd., Tokyo, Japan Studies on general pharmacology of L-DOPA. *Annual Report of Sankyo Research Laboratories (Tokyo).* 22:123-141, 1970.

The general pharmacological effects of L-Dopa are presented, based on experiments on many animals. L-Dopa induces a significant increase of locomotor activity, mydriasis and potentiation of thiopental anesthesia in mice. Analgesic and anticonvulsant actions are not observed. In rats, L-Dopa induces an increase of locomotor activity, salivation, piloerection, hyperthermia and hypertension. L-Dopa antagonized the hypoactivity, hypothermia and hypotension in animals pretreated with reserpine. Conditioned avoidance response, pupillary size and the movement of the uterus of pregnant animals are not influenced by L-Dopa. Ptosis, catalepsy and miosis produced by reserpine are not antagonized by L-Dopa. No antispasmodic effects of L-Dopa are observed in isolated guinea pig ileum. In anesthetized dogs doses of 3 to 30mg/kg of L-Dopa intravenously administered causes hypertension, increase in heart rate and stimulation of respiration according to the dosage. Thirty mg/kg of L-Dopa induces sinus arrhythmia in many cases but this arrhythmia disappeared when the blood pressure returned to normal. 24 references.(Author abstract modified)

131057 Nakanichi, Michio; Okada, Tadao; Kato, Yasuyuki. Research Laboratories, Yoshitomi Pharmaceutical Industries, Ltd., Japan Studies on psychotropic drugs (sixth report) - metabolic fate of APY-606 - excretion and metabolism in rats. *Journal of the Pharmaceutical Society of Japan (Tokyo).* 90(7):808-812, 1970.

The metabolic fate of APY-606 in rats was studied. Following administration of the drug, a quantitative determination of the drug in rat urine was made using spectrophotometric methods. Less than 1.5% of the given dose was found in the urine during the three days following drug administration. One of the four metabolites of APY-606 detected in rat urine by thin layer chromatography was phenothiazine s-oxide of APY-606. Another compound with an hydroxy group was detected with a color reaction test. Three additional metabolites were also detected in the bile, however the native compound was not found. 12 references. (Author abstract modified)

131058 Nakanishi, Michio; Okada, Tadao; Tsumagari, Tatsumi. Research Laboratories, Yoshitomi Pharmaceutical Industries, Ltd., Japan Studies on psychotropic drugs (fifth report) -- pharamcological effect of 8(3-(2-chloro-10-phenothiazinyl)propyl)-1-thia-4,8-diazaspir ro(4,5)decan-3-one hydrochloride (APY-606). *Journal of the Pharmaceutical Society of Japan (Tokyo).* 90(7):800-807, 1970.

The pharmacological activity of 8-(3-(2-chloro-10-phenothiazinyl)propyl)-1-thia-4,8-diaspiro(4,5)decan 3none hydrochloride (APY-606), a new derivative of phenothiazine, was compared to chlorpromazine and thioridazine in rats. APY-606 had a potent sympatholytic action with a low toxicity although it is a phenothiazine derivative and showed a characteristic spectrum of pharmacological activities which differed from that of standard compounds. Application of the drug as a psychotropic drug in clinical use is suggested. (Author abstract modified)

131059 Imamura, Hiroshi; Okada, Tadao; Matsui, Eiichi; Kato, Yasuyuki. Research Laboratories, Yoshitomi Pharmaceutical Industries, Ltd., Japan Studies on psychotropic drugs (seventh report) -- metabolic fate of APY-606 -- absorption, distribution, excretion and metabolism of tritiated APY-606. *Journal of Pharmaceutical Society of Japan (Tokyo).* 90(7):813-817, 1970.

The absorption, distribution, excretion and metabolism of tritiated APY-606 (3H-APY-606), a new phenothiazine derivative was studied in rats. When the compound was orally administered at a dose of 10mg/kg, 40% of the dose was absorbed from the gastrointestinal tract within six hours. Of the administered radioactivity (3H), 3% and 55% were excreted in the urine and feces, respectively, during the three days following the oral administration of 3H-APY-606; 32% of the dose was excreted in the bile within 24 hours. The highest concentration of 3H was found in the liver, adrenals, kidney and lung four hours after its administration. Radioactivity level in the brain was two to four times as high as that in the blood. Ninety percent of the 3H in the serum was bound to protein after one hour and 34% was bound after 24 hours. seventy percent of 3H in the urine and 94% of it in the bile were extracted with organic solvent, and a small amount of glucuronide was formed in the urine; four radioactive metabolites in the urine and three metabolites in the bile were detected by thin layer chromatography, but the native compound was not detected. 12 references. (Author abstract modified)

03 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

100852 Watanabe, Shosuke; Mitsunobu, Katsusuke; Sannomiya, Takanori; Otsuki, Saburo. Dept.of Neuro-Psychiatry, Okayama University Medical School, Okayama, Japan L-0U-14C0 tyrosine metabolism of the perfused cat brain with high plasma phenylalanine or without plasma tyrosine. *Folia Psychiatrica et Neurologica Japonica (Tokyo).* 24(4):219-226, 1970.

Cat brain perfusion was carried out with standard artificial blood containing 2mg/dl of L-tyrosine and also with standard blood not containing tyrosine, for 70 minutes in each group. Another group was perfused with the tyrosine containing artificial blood plus 50 mg/dl of L-phenylalanine. Each of these experiments was conducted to see how such blood would affect the tyrosine metabolism of the brain. In the perfusion without addition of tyrosine, the tyrosine content of the brain decreased markedly. Further, there was an outflow of the brain tyrosine into the venous blood. The free tyrosine of the brain is mainly supplied from the blood tyrosine. In the high plasma phenylalanine perfusion, the transport of the blood tyrosine into the brain was inhibited competitively by the blood phenylalanine, but output of tyrosine from the brain to the blood was not disturbed. In the high plasma phenylalanine perfusion, the incorporation of tyrosine into the brain protein fraction from the brain acid soluble fraction was lower than that of the control group. During the high plasma phenylalanine perfusion, there was observed a marked increase of phenylalanine, and a decrease of tyrosine, threonine, isoleucine and leucine in the brain. 20 references. (Author abstract modified)

101006 Khristolyubova, N.A. Tsentr.Nauch.-Issled.Institut Sudebnoy Psikhiatrii im.Prof. Serbskogo Ministerstva Zdravodkhraneniya SSSR, Moscow /The effect of diethylamide of lysergic acid (DLA) on the content of monoamines in some nuclei of the mid-brain and hypothalamus./ Vliyaniye dietilamida lizerginovoy kisloty (DLK) na soderzhaniye monoaminov v nekotorykh yadrakh srednego mozga i gipotalamusa. *Byulleten' Eksperimental'noy Biologii i Meditsiny (Moskva).* 70(9):53-55, 1970.

Fifteen and 60 min after LSD injection (doses of 20 and 30mg/kg) and 19 hr after LSD injection (0.2to 1.2mg/kg) in the reticular formation of the midbrain on the level of the caudal interpeduncular nucleus, in substantia nigra, in the zone above the interpeduncular nucleus on the level of its third median and in the area situated laterally from the interpeduncular nucleus on the level of

its third cranial, a distinct increase in the content of catecholamines is observed in rats. In the paraventricular, supraoptic and dorsomedial nucleus of the hypothalamus, in 60 min a reduced concentration of catecholamines was noted when LSD was introduced in a dose of 20mg/kg. After LSD injection (20 or 30mg/kg), in 15 min, definite changes in the content of monoamines could not be revealed. 13 references. (Author abstract)

101316 Richter, Judith A.; Goldstein, Avram. Department of Pharmacology, Stanford University, Stanford, Calif.94305 Effects of morphine and levorphanol on brain acetylcholine content in mice. ***Journal of Pharmacology and Experimental Therapeutics.*** **175(3):685-691, 1970.**

Effects of morphine and levorphanol on brain acetylcholine content in mice were investigated. A modest increase in brain acetylcholine was demonstrated with both morphine and levorphanol. It occurs in the 'free' and 'bound' fractions of acetylcholine but usually is largest and most significant in the latter. Similar increases were found in the pooled cerebral cortex and cerebellum and in the rest of the brain when these regions were examined separately. The inert stereoisomer dextrorphan, at a dose equal to an effect dose of levorphanol, did not cause an increase in brain acetylcholine. In mice made tolerant to the analgesic effect of levorphanol by repeated injection, only a small increase in brain acetylcholine occurred. 20 references. (Journal abstract modified)

104737 Chinn, Chung. University of Washington A pharmacological study of the anti-muscarinic actions of several antidepressants. (Ph.D.dissertation). ***Dissertation Abstracts International.*** **Ann Arbor, Mich., Univ.M-films, No.71-16931 HC$10.00 MF$4.00 128 p.**

A pharmacological study of the antimuscarinic actions of several antidepressants on cats was made. Selected psychostimulants or antidepressants utilized included: methylphenidate, pheniprazien, desipramine, amitriptyline. Based on the similarity between muscarinic responses in sympathetic ganglion cells and cells of the central nervous system, the specific antimuscarinic action of these antidepressants in the superior cervical ganglion suggests such an action in the central nervous system. Antagonism by the selected antidepressant agents of the hypothermia and tremors produced by oxotremorine strengthen such a conclusion. Since centrally administered muscarinic stimulants produce increased parasympathetic outflow, the results allow the conclusion that antidepressants may inhibit this outflow, resulting in atropine-like effects in the peripheral autonomic nervous system. (Journal abstract modified)

105620 Khaunina, R.A. Leningradskogo Nauchno-Issledovatel'skogo Psykhonevrologicheskogo Instituta IM.V. M.Bekhtereva, Leningrad, U.S.S.R. /Participation of serotoninergic processes in the action of phenigama./ Uchastiye serotoninergicheskikh protsessov v deystvii fenigamy. ***In: Lapin, I., Serotoninergic Processes in the Action of Psych.Drugs.*** **Leningrad, RSFSR Ministry of Health, 1970.237 p.vol.53 (p.77-87).**

The action of phenigama (beta-phenyl-gamma-aminobutyric acid) on the effects of 5-HTP was investigated in mice. Phenigama in a dose of 200mg/kg suppressed the 5-HTP, induced head twitches and did not influence its hypothermic action and diarrhea. Phenigama also did not influence these effects of serotonin. In a dose of 200mg/kg, phenigama did not change the level of 5-HT and norepinephrine in the brain. Intraperitoneal injection of 5-HTP increased the level of 5-HT in the brain, and phenigama lowered this increase to 33%. These effetcs of phenigama may be explained by its hypothermic action, as the warming of the mice abolished its effect. The 5-HTP in a dose of 125mg/kg increased the level of 5-HT in the brain to the same level, as 5-HTP in a dose of 125mg/kg together with phenigama did. However, in the first case, 5-HTP induced head twitches did exist, and in the second, they were suppressed. Phenigama in a dose of 200mg/kg de-creased motor activity, coordination of movements and muscle tonus. The ability of phenigama to suppress the 5-HTP and produce head twitches is related more to its nonspecific depressive action, than to its specific antiserotonin action. 15 references. (Author abstract)

105720 Eshchanov, T.B. TsNIL Samarkandskii meditsinskii institut, Samarkand, UzSSR /Effect of capers on the vascular lumen of isolated extremities of sensitized frogs and the antianaphylatic effect of suprastin./ Vliianie kapertsev na prosvet sosudov isolirovannyky konechnostei sensibilizirovannykh liagushek i antianafilakticheskoe deistvie suprastina. ***Meditsinskiy Zhurnal Uzbekistana.*** **11:30, 1970.**

In a pharmacological investigation of the desensitizing properties of prickly capers, the effectiveness of various concerntrations of decoction of capers during anaphylaxis in frogs was established. Study of the antianaphylactic effect of suprastin, a Hungarian preparation, indicated its clearly expressed influence on sensitized guinea pigs. All results were statistically confirmed. (Journal abstract modified)

105721 Polievtsev, N.P.; Evdokimova, N.I.; Sultanov, M.B. author address not given /Influence of Haplophyllum alkaloids on the body temperature of animals./ Vliianie alkaloidov Haplophyllum na temperatury tela zhivotnykh. *Meditsinskiy Zhurnal Uzbekistana*. 11:28-29, 1970.

Experiments were conducted with 500 mice to investigate the influence of Haplophyllum alkaloids in affecting body temperature under conditions of varying environmental temperatures. In separate trials, the effects of alkaloids on the hypothermic action of aminazine and on the hyperthermic activity of phenamine were studied. The hypothermic effect of alkaloids was found to increase not only with an increase in dosage of these substances but also with a decrease in temperature of the surroundings. When alkaloid dosages were administered against a background of aminazine, a marked synergetic effect was noted in all cases. Phenamine provoked acute hyperthermia, particularly within the first hour following administration. Administration of a combined dosage of the alkaloid and phenamine caused the same effect observed in the recipients of phenamine alone. The results suggest the presence of mutual antagonism between the hyperthermic property of phenamine and the hypothermic action of the Haplophyllum alkaloids.

106270 Ishihara, Ichiro; Yokoo, Yuriko. Nagoya University, Nagoya, Japan Adrenal cortical and medullary secretion and evaluation of drugs acting on the central nervous system. *Annual Report of the Research Inst.of Environmental Medicine, Nagoya Univ.* 18(7):7-21, 1970.

The changes of the adrenal cortical and medullary secretions were investigated in dogs having a retention cannula in the adrenal vein after the administration of some of the drugs acting on the CNS, pyrithioxin, meclofenoxate, GABA and cytidine diphosphate choline. These drugs were recognized to have a characteristic effect on secretion patterns of these endocrine systems. Pyrithioxin caused an immediate, marked increase of adrenocortical secretion of corticosteroid resistant type, and simultaneously an intense stimulation of adrenomedullary secretion. Meclofenoxate HCl also induced an immediate, marked and lasting increase of adrenocortical secretion consisting of both corticosteroid sensitive and resistant components. The adrenomedullary response was also prompt and marked. GABA caused relatively mild but lasting increase of adrenocortical secretion consisting of both sensitive and resistant components. The remarkable and prolonged elevation of adrenomedullary secretion occurred, but it was suppressed by cortisol pretreatment. Cytidine diphosphate choline had little effect on these endocrine secretions. These secretion patterns indicate the primary action of the drugs on certain structures in the CNS. The physiological and pharmacological implications of these results are discussed 20 references. (Author abstract)

106780 Mellerup, E.T.; Plenge, P.; Ziegler, R.; Refaelsen, O.J. Psychochemistry Institute, University Department of Psychiatry, Rigshospitalet, 9, Blegdamsvej, DK-2100 Copenhagen, Denmark Lithium effects on calcium metabolism in rats. *International Pharmacopsychiatry (Basel)*. 5(2-4):258-264, 1970.

Administration of lithium chloride to rats increased serum calcium. The distribution of injected calcium-45 was changed by lithium: radioactivity in serum was increased, radioactivity in bone was decreased. It was shown that the effect of lithium was independent of secretion of calcitonin, parathyroid hormone, and glucagon. 10 references. (Journal abstract)

106783 Wagner, B.M.; Cooper, T.B.; Kline, N.S. Francis Delafield Hospital Division, Columbia-Presbyterian Medical Center, Columbia University, New York, N.Y. Structural basis of lithium psychopharmacology: extracellular ground substance of rat brain. *International Pharmacopsychiatry (Basel)*. 5(2-4): 208-217, 1970.

The extracellular ground substance in brains of rats treated with lithium was studied. Relatively little attention has been given to the possible role of the cerebral extracellular matrix as a site of drug action. Accumulated neurophysiological, biochemical and cytological data suggest the attractive hypothesis, that the pericellular environ-

ment may be critical to the integrity of the neuron. Analogy to the role of the extracellular ground substance in the heart and kidney leads to the suggestion of a similar function in the brain. Lithium as an effective psychoactive drug lends itself to a detailed study of this system in the brain. Further application of histochemistry, election microscopy and microchemistry to the problem may serve to elucidate the mechanism of lithium action. 35 references. (Author abstract modified)

107190 Hirose, Akimune. Kyoto Prefectural University of Medicine, Japan Central action of some autonomic drugs in respect to EEG arousal reaction of the rabbit. ***Journal of Kyoto Prefectural University of Medicine (Kyoto).*** **79(9):707-719, 1970.**

A report on the central action of autonomic drugs, such as arecoline, benactyzine, hiropon, and phenoxybenzamine, as it affects the EEG arousal reaction, is presented. The report is based on the experiment of applying these drugs to the cortical sensorimotor areas of unanesthetized rabbits in a small plot of filter paper or by intravenous injection. Some of the results show: the injection of arecoline and hiropon induces the desynchronization of EEG waves and lowers the threshold of the arousal reaction elicited by reticular stimulation; injection of benactyzine and phenoybenzamine induces the synchronization of EEG waves and elevates the threshold of the arousal reaction elicited by reticular stimulation; injection of benactyzine antagonizes the desynchronization after the injection of hiropon, but hiropon does not antagonize the synchronization after the injection of benactyzine; the injection of arecoline antagonizes the synchronization after the injection of phenoxybenzamine, but phenoybenzamine does not antagonize the desynchronization after the injection of arecoline. The conclusion, from these results are: the terminal of the ascending pathway from reticular formation to cerebral cortex seems to be cholinergic, and the adrenoreactive system seems to play an important part in the metabolic process of cortical cells under the desynchronization of EEG waves. 32 references. (Author abstract modified)

108694 Stanislawska, Jolanta; Wajszczuk-Religa, Anna. Dept.of Human Physiology, Medical Academy, Krakowskie Przedmiescie Str.No.26/28, Warsaw, Poland Anti-serotonin effect of agents blocking the adrenergic beta-receptor. ***Acta Physiologica Polonica (Warszawa).*** **21(6):627-633, 1970.**

The antiserotonin effect of beta-receptor blocking agents (Alderlin, Inderal and DCI) was studied on preparations of isolated guinea pig ileum. All compounds inhibited the constricting action of serotonin. The antiserotonin effect of these drugs lasted 10 to 30 min. It was found that the inhibitory effect was connected with both D-type and M-type receptors. For this purpose receptor D was blocked by adding LSD to the bath containing the intestine, while receptor M was blocked by morphine. The character of inhibition by 3 beta blockers under investigation of the serotonin constricting action is difficult to interpret. The shift of curves expressing the dose - response relationship after application of blockers did not fully confirm the competitive nature of blocking. It is suggested that this mechanism is directly connected with the serotonin receptor, and the antiserotonin effect of beta blockers is related to their inhibiting action on adenycyclase. 8 references. (Author abstract modified)

110631 Gusel', V.A. Kafedra farmakologii Leningradskogo pediatricheskogo instituta, Leningrad, USSR /Effect of agents interacting with cholino-and adrenoreactive systems on epileptiform activity in the hippocampus of rabbits./ Vliyaniye sredstv, vzaimodeystvuyushchikh s kholino- i adrenoreaktivnymi sistemami, na epileptiformnuyu aktivnost' v gippokampe krolikov. ***Farmakologiya i Toksikologiya (Moskva).*** **33(4):406-411, 1970.**

An investigation was carried out on rabbits with chronically implanted electrodes and a chronic epileptogenic zone in the hippocampus, reproduced by following a modified method of Kopelov. The experiments showed that galanthamine and pyridrol, as well as sound stimuli, blocked sporadic epileptiform discharges and simultaneously induced electroencephalographic activation reaction. With the hippocampus becoming the scene of intensive epileptiform activity in the form of high range 2 phase peaks continuously succeeding each other (without generalization from the hippocampi and any behavioral manifestations), neither the sound stimuli nor galanthamine or pyridrol induced any electroencephalographic activation reaction nor did they affect pathological activity. Metamizyl intensified and chlorpromazine suppressed epileptiform activity. 24 references. (Journal abstract modified)

110632 Cherkes, A.I.; Frantsuzova, S.B. Kafedra farmakologii Kiyevskogo meditsinskogo instituta, Kiev, USSR /Effect of ganglionic blocking agents on pressor effects of sympathomimetic amines of direct and indirect action./ Vliyaniye gangiolitikov na pressornyye effekty simpatomimeticheskikh aminov pryamogo i nepryamogo deystviya. *Farmakologiya i Toksikologiya (Moskva).* 33(4):411-414, 1970.

Experiments on cats anesthetized with urethan showed that preliminary administration of ganglionic blocking agents, pyrilene (1, 2, 2, 6,6-pentamethylpiperidine toluene sulfonate) and hexamethonium (1,6 bis-N-N-N-trimethyl ammonium hexane diiodide) significantly increases the pressor response to sympathomimetic amines of direct (noradrenaline) and indirect (tyramine) effect. The hypotensive effect of pyrilene in cats pretreated with reserpine is 3 times lower than that in intact animals. The response pressor reaction to tyramine in cats treated with reserpine is also significantly lower. 10 references. (Journal abstract modified)

110633 Fomochkin, I.P. Kafedra farmakologii Krymskogo meditsinskogo instituta, Simferopol', USSR /Effect of antidepressants on cerebral circulation and oxygen uptake./ Vliyaniye antidepressantov na mozgovoye krovoobrashcheniye i pogloshcheniye kisloroda mozgom. *Farmakologiya i Toksikologiya (Moskva).* 33(4):426-428, 1970.

The effect of melipramine (2.5mg/kg), transamine (1.25mg/kg) and iprazid (5mg/kg) on the cerebral circulation and oxygen uptake by the brain was studied in acute tests performed on dogs under sodium - ethaminal anesthesia. Oxyhemography, polarography and continuous measurement of the rate at which the blood flowed out of the brain sinuses were used to determine the effects. The findings indicate that oxygen uptake by the brain increases and cerebral circulation decreases under the effect of melipramine and transamine. In most experiments iprazid increased cerebral circulation and decreased oxygen uptake by the brain. (Journal abstract modified)

111767 Gabriyelyan, E.S.; Virabyan, T.L. Kafedra farmakologii Yerevanskogo meditsinskogo instituta, Yerevan, Armenian SSR /Effect of ganglerone and quaterone on catecholamine content in the brain./ Vliyaniye ganglerona i kvaterona na soderzhaniye katekholaminov v golovnom mozgu. *Zhurnal Eksperimental'noy i Klinicheskoy meditsiny (Erevan').* 10(6):12-15, 1970.

Experiments were conducted on 64 white rats to study the effect of ganglerone and quaterone, containing tertiary and quaternary nitrogen, on the level of catecholamines in the brain. Adrenalin and noradrenalin levels were determined with the aid of a spectrophotofluorometer. The data obtained indicate that the N-cholinolytic agents, depending on the amount injected, have a different effect on the levels of adrenalin and noradrenalin in the brain and on the change in catecholamine levels in the cerebral cortex and hypothalamus. Ganglerone and quaterone differ considerably in their effects on catecholamine levels. The increase in the tonus of cerebral vessels under the effect of small doses of ganglerone is explained by its capacity to increase secretion of noradrenalin and this is expressed in an increase of resistance of the cerebral vessels and a decrease of cerebral circulation. 4 references.

114975 Takatsuka, Katsuya; Segawa, Tomio; Takagi, Hiroshi. Dept.of Pharmacology, Faculty of Pharmaceutical Sciences, Kyoto University, Sakyo-ku, Kyoto, Japan Uptake and storage mechanism of 5-hydroxytryptamine in rabbit brain stem and effect of reserpine. *Japanese Journal of Pharmacology (Kyoto).* 21(1):57-67, 1971.

The role of 5-hydroxytryptamine(5-HT) in synaptic transmission, especially in central nervous system, was investigated through experiments on 5-HT uptake by subcellular fraction of rabbit brain stem. When the rabbit was treated with monoamine oxidase inhibitor (MAOI) alone or pretreated with MAOI followed by 5-hydroxytryptophan(5-HTP) marked increase in 5-HT concentration in P3, S3, P2A and P2B fraction from brain stem was observed. P1 fraction could take up 5-HT in vitro but the uptake was temperature insensitive and nearly all of 5-HT taken up at 37 deg C could be readily washed out. The uptake of 5-HT by P2 fraction was temperature dependent and the amine taken up at 37 deg C could not easily be removed by washing. P3 fraction also took up 5-HT in similar fashion. 5-HT bound to P2 fraction in vitro was found to be mainly associated with P2V fraction and was more concentrated than in P2 fraction. The rate of uptake of 5-HT by sv was fast. At low 5-HT concentration in medium the amount of 5-HT taken up by P2V and P2S fraction was almost proportional to 5-HT concentration in medium. P2 fraction, when incubated with 5-HTP took up less amount of 5-HT. The uptake of 5-HT by P2V fraction was affected

by pH, it increased with increasing pH of the medium, decreased with decreasing pH of the medium. Reserpine was found to act mainly at the level of sv. 31 references. (Author abstract modified)

114978 Madan, B.R.; Madan, V. Dept.of Pharmacology, Sardar Patel Medical College, Bikaner, Rajasthan, India Effect of two recently synthesized phenothiazine derivatives upon experimental cardiac arrhythmias. *Japanese Journal of Pharmacology (Kyoto).* 21(1):41-46, 1971.

Two new phenothiazines, benzosulfonate and piperacetazine, have been investigated for their antiarrhythmic activity in the dog. They are effective in reducing the duration of acetylcholine induced atrial fibrillation, in establishing the end point in aconitine induced atrial arrhythmia and in reverting the injury stimulation induced atrial flutter to normal sinus rhythm. Also, they cause significant attenuation of ventricular ectopic activity following 2 stage ligation of the anterior descending branch of the left coronary artery. On the basis of their toxicity studies and efficacy, it is suggested that piperacetazine may be useful in the clinic in the treatment of cardiac arrhythmias. 24 references. (Author abstract)

116471 Downes, Hall; Perry, Roger S.; Ostlund, Richard E.; Karler, Ralph. Dept.of Pharmacdogy, Univ.of Oregon Medical School, 3181 S.W. San Jackson Park Road, Portland, OR 97201 A study of the excitatory effects of barbiturates. *Journal of Pharmacology and Experimental Therapeutics.* 175(3):692-699, 1970.

To determine whether 5-(2-cyclohexylideneethyl)-5-ethyl barbituric acid (CHEB) produces CNS effect distinctly different from those produced by the more frequently studied convulsant barbiturates, such as the (+)-isomer of 5-(1,3-dimethylbutyl)-5-ethyl barbituric acid (DMBB), i.v.administration of CHEB and DMBB was studied in mice. Both CHEB and DMBB induced tonic extensor seizures preceded by brief tonic flexion. No evidence of depression preceded or accompanied these seizures. In contrast, the (-)-isomer of DMBB induced preanesthetic excitation without tonic seizures and antagonized the seizure activity of the (+)-isomer. (-)-DMBB was slightly more potent than pentobarbital as a central nervous system depressant and had an LD50 over 20 times higher than (+)-DMBB. Depressant barbiturates were more effective antagonists of barbiturate induced convulsions than were trimethadione and diphenylhydantoin. Phenobarbital was an effective antagonist at 6.6% of its neurotoxic dose 50. Barbiturates that caused preanesthetic excitation without tonic seizures produced simple depression at lower doses than those needed to elicit preanesthetic excitation. On the basis of these studies it is concluded that the depression which accompanies the seizure activity of racemic DMBB is not a necessary concomitant of barbiturate excitation and obscures the full convulsant effect. 27 references. (Journal abstract)

120465 Javoy, F.; Glowinski, J. Groupe N. B., Laboratoire de Biologie Moleculaire, College de France, France Dynamic characteristics of the 'functional compartment' of dopamine in dopaminergic terminals of the rat striatum. *Journal of Neurochemistry.* 18(7):1305-1311, 1971.

Examination of the diappearance of dopamine in the striatum of rats injected with alpha-methyl-p-tyrosine is reported. Two main phases of dopamine decline were detected which probably correspond to the amine utilization in a functional and a main storage compartment in dopaminergic terminals. In control rats the half lifes of dopamine were about 9 and 120 min in the functional and main storage compartments respectively. The rate of dopamine synthesis was estimated to be not less than 13.2micrograms/gh and the rate of dopamine utilization in the functional compartment was calculated to be about 4 times that of the main storage compartment. 9 references. (Author abstract)

130422 Sasajima, Michitada. Department of Pharmacology, School of Medicine, Keio University, Tokyo Analgesic effect of morphine hydrochloride injected directly into the ventricle of mouse brain. *Journal of the Keio Medical Society (Tokyo).* 47(5):525-531, 1970.

A report on analgesic effects of morphine hydrochloride injected directly into the ventricle of mouse brain is presented, including an examination of the distribution of the drug by using India ink, the determination of the minimum effective dose of the drug for analgesia by various methods of measurement, and evaluation of the blind test. The results show: the drug is detected almost exclusively in the ventricles of mice after interacerebral injection by the Haley and McCormick Method; small quantities of the drug induce

sedation and analgesia and large quantities of excitation; the minimum dose of morphine hydorchloride to produce analgesic response is estimated to be 100, 10, 1.0, 0.1micrograms per mouse by Haffner's hot plate, pressure, and writhing syndrome methods, respectively; the blind test method is indispensable for getting unbiased data on various analgesic tests. 10 references. (Author abstract modified)

130427 Anan, Ichiro. Department of Pharmacology, School of Medicine, Keio University, Tokyo Changes of the body temperature of codeine tolerant rats by the administration of nalorphine. ***Journal of the Keio Medical Society (Tokyo).*** **47(5):555-560, 1970.**

A report on a new method for screening the dependence producing liability of codeine by administration of nalorphine is presented, based on an experiment where rats were administered codeine hydrochloride two to three times daily for three to seven weeks and measured for body temperature after the subcutaneous injection of nalorphine. The significant decrease in body temperature and body weight was observed in every rat. Since the injection of nalorphine does not affect the body temperature of normal rats, the change in body temperature of codeine tolerant rats is considered to be one of the indicators of physical dependence formation of the morphine type. The possibility of adapting this indicator as a new screening method is suggested. 1 reference. (Author abstract modified)

131623 Narumi, Shigehiko; Suzuki, Yukiko; Hana, Kotobuki. Faculty of Pharmaceutical Sciences, Osaka University, Japan Electroencephalographic effects of atropine and scopolamine. ***Journal of the Pharmaceutical Society of Japan (Tokyo).*** **90(6):651-660, 1970.**

The electroencephalographic effects of atropine and scopolamine on cats, dogs, rabbits, guinea pigs, rats, and mice were studied. In addition, the behavioral and convulsive effects of nikethamide, pentetrazol, and acetylcholine were examined. Atropine and scopolamine caused bursts of 15-16 Hz spindle waves or high voltage slow waves in the cortical and subcortical EEGs of all species except the guinea pig. Scopolamine caused high voltage slow waves in the guinea pig. Nikethamide induced convulsive behavior and spike or seizure patterns in EEGs in all species except the guinea pig; pretreatment with atropine suppressed these effects. Pentetrazol induced convulsive behavior and spike or seizure patterns in the EEGs of rabbits and cats while neither atropine nor scopolamine had any effect. Intracisternal injection of acetylcholine into curarized cats induced an EEG spike pattern that was suppressed by atropine and scopolamine. It is concluded that the difference between atropine and scopolamine lies in their suppressive effect in the convulsions induced by nikethamide. (Author abstract modified)

04 MECHANISM OF ACTION: BEHAVIORAL

103267 Adams, Perrie Milton. Florida State University An analysis of the role of cholinergic drugs in behavior related to food and water deprivation. (Ph.D.dissertation). ***Dissertation Abstracts International.*** **Ann Arbor, Mich., Univ.Mfilms, No.71-13484 HC$10.00 MF$4.00 99 p.**

A study designed to investigate the effects of cholinergic drugs on behavior related to food and water intake under different deprivation conditions is reported. The effects of a cholinomimetic, 2 cholinolytics, and 2 cholinesterase inhibitors on rats were analyzed. The effects of the cholinergic drugs were found to be significantly affected by the deprivation condition of the organism. All drugs were found to affect both food and water related dependent measures. There was some evidence of a greater effectiveness with the drugs having central action.

103350 Kanzler, Alfred W. Claremont Graduate School and University Center Alcohol as a discriminative stimulus in the conditioned emotional response. (Ph.D.dissertation). *Dissertation Abstracts International.* Ann Arbor, Mich., Univ.M-films, No.71-13705 HC$10.00 MF$4.00 87 p.

It was hypothesized that alcohol acts as a discriminative stimulus, similar to those stimuli used in external stimulus control. To test the hypothesis, 20 rats were trained to barpress in a Skinner Box to a FR 12 schedule of reinforcement under nonalcoholic conditions. Ten of these subjects were then injected with alcohol and received 16 buzzer footshock pairings in a separate compartment over a 2 day period. The other 10 subjects received similar treatment after saline injections. The subjects were then tested with counterbalanced drug conditions. The analysis of the ratio scores indicated that discrimination between states had occurred after the first conditioning trials, and generalization between the states after the second conditioning trials. It was concluded that discrimination is a more appropriate explanation for the overserved changes than a state dependent hypothesis. A second part of the experiment was concerned with the consistent findings that subjects trained without alcohol and subsequently tested under alcohol display higher response rates in the Skinner box. Experiments showed that the novelty hypothesis does not explain this behavior. (Journal abstract modified)

103354 Guth, Sheila. University of California, Los Angeles Comparison of the effects of exogenous ACTH on approach and avoidance conditioning: implications for the physiology of incentive motivation. (Ph.D.dissertation). *Dissertation Abstracts International.* Ann Arbor, Mich., Univ.M-films, No.71-13998 HC$10.00 MF$4.00 110 p.

The effects of exogenous ACTH on approach and avoidance conditioning were compared in rats and implications drawn concerning the physiology of incentive motivation. In 3 studies, it was found a) that exogenous elevation of adrenocorticotropic hormone (ACTH) in rats during acquisition of a lever press response for water, led to a higher asymptotic response rate and greater resistance to extinction; b) in an approach - avoidance conflict situation a single injection of ACTH 10 minutes before the punishment trial led to increased suppression of the approach response; c) injection of ACTH during acquisition of a simple approach to water, initally augmented and then facilitated recovery from effects of subsequent punishment, and, d) ACTH administered during extinction of the lever-press response had no effect, whereas the same treatment retarded recovery from punishment. Plasma corticosterone levels were measured at several time points before and after a behavior session. It was found that in control animals performing a response for water on a fixed daily schedule, there is a gradual rise in endogenous ACTH as measured by the corticoids released, beginning at least 5 hours before the session. This rise peaks at one hour before the session and is followed by a sharp drop after the session. Repeated daily injections of ACTH were found to reduce the endogenous hormone release at all time points, and to greatly increase both the speed and final level of the corticoid response to the injection. It was pointed out that this constellation of effects cannot be handled by either the fear or the disinhibition hypothesis of action of ACTH. ACTH may instead operate to increase the incentive supports of adaptive behavior. (Journal abstract modified)

103710 Cox, Raymond H., Jr. Indiana University Comparative study of CNS stimulatory activity and anorexigenic potency of phenylethylamine derivatives. (Ph.D.Dissertation). *Dissertation Abstracts International.* Ann Arbor, Mich., Univ.M-films, No.71-12451 HC$10.00 MF$4.00 109p.

Results of a comparative study of CNS stimulatory activity and anorexigenic potency of phenylethylamine derivatives are presented. Several of these compounds were compared in a free feeding situation and a continuous avoidance schedule to assess their effects on food intake and behavior in a variety of species. Particular attention was paid to the structure of these drugs and anorectic versus stimulatory actions are also discussed. Also an attempt was made to assess the effects in inhibiting NE synthesis with alpha-methyltyrosine on the action of these agents. Results indicate that in the case of amphetamine and benzphetamine increasing the cyclic AMP levels has no effect on their anorectic action. However, in the case of their para substituted derivatives, caffeine was shown to potentiate their anorectic action. Thus, the possibility is raised that these compounds may have an action on cyclic AMP which mediates their anorectic action. One conclusion that can be drawn from the data is that the para substituted compounds have a mechanism of anorectic action at least partially different from their unsubstituted analogues. Support for such a proposal for the p-

chloro analogue of amphetamine comes from several studies which show that the CNS stimulation elicited by these compounds are very likely mediated via different mechanisms. (Journal abstract modified)

105621 Lapin, I.P. Laboratoriya Psikhopharmakologii Leningradskogo Nauch.-Issled. Psikhonevrologicheskogo Instituta im.V. M.Bekhtereva, Leningrad /Does kynurenine possess any neurotropic activity?/ Obladayet li kinurenin neyrotropnoy aktivnost'yu? *In: Lapin, I., Serotoninergic processes in the action of psych.drugs.* Leningrad, RSFSR Ministry of Health, 1970. 237 p. v.53 (p.113-138).

Intraperitoneal or subcutaneous injections of DL-kynurenine, a metabolite of tryptophan, did not produce any visible behavioral effects in mice (10 to 400mg/kg) and rats (10 to 100mg/kg). Pretreatment with pyridoxine (vitamin B6), p-chlorophenylalanine, an inhibitor of tryptophan hydroxylase and selective depletor of brain serotonin, and phenelzine, an inhibitor of monoamine oxidase, did not manifest any action of kynurenine. Injections of kynurenine (50 and 100mg/kg) decreased the number of tryptophan produced head twitches in mice and rats and lowered toxicity of 5-hydroxytryptophan. Kynurenine did not change pharmacological effects of amphetamine, reserpine and reserpine-like drug RO 4-1284. Kynurenine (0.2andno- grams to 200mcg, I.V.)lowered blood pressure in anesthetized rats and diminished the pressor effect of serotonin (0.5to 5mcg). Kynurenine possesses weak neurotropic activity and, if that activity is of importance, it could have an adaptogenic function. 21 references. (Author abstract)

110682 Balster, Robert Louis. University of Houston The effectiveness of external and drug produced internal stimuli in the discriminative control of operant behavior. (Ph.D.dissertation). *Dissertation Abstracts International.* Ann Arbor, Mich., Univ.M-films, No.71-3951 HC$10.00 MF$4.00 149 p.

A comparison was made between the effectiveness of external cues and drug produced internal cues to exercise stimulus control over food reinforced operant behavior in the albino rat. Two external stimulus groups used either the presence or absence of a change in illumination provided by turning on 2 cue lights or the presence or absence of a 1000 Hz.tone as cues. A mixed schedule control group was also included. Two operant discrimination procedures were utilized, the first of which was a 2 lever multiple schedule with each of the 2 cues in each group associated with responding on 1 of the levers. Results indicated that the control and external stimulus groups did not differ, whereas each of 2 drug groups demonstrated more effective stimulus control. Ss were then transferred to a 2 level mixed schedule during which correct lever responses were reinforced on a variable interval 30 sec schedule. Stimulus control to the external stimuli was again not observed, while pentobarbital produced cues (1 of the 2 drug groups) demonstrated weak but significant stimulus control over lever choice. Amphetamine produced cues gave strong residual stimulus control over both lever choice and response patterning. Results are discussed in terms of the importance of reinforcement feedback cues which apparently interfered with the development of stimulus control by the external stimuli. Possible explanation for the superior effectiveness of drug cues are discussed and the relationship of this finding to a conditioning model of drug abuse is considered. (Journal abstract modified)

110906 Hirtzel, Mari Sylvie. University of Michigan Stimulus properties of electroconvulsive shock in goldfish. (Ph.D.dissertation). *Dissertation Abstracts International.* Ann Arbor, Mich., Univ.M-films, No.71-4635 HC$10.00 MF$4.00 77 p.

Electroconvulsive shock (ECS) was administered to goldfish in conjection with 2 behavioral situations. In the first set, the ECS was given immediately or 24 hours after 1 trial positive conditioned suppression training. Amnesia for the training was produced by the immediate treatment. In the second set, ECS was administered immediately after a baseline session in which fish responded on an intermittent schedule of food reinforcement. A reversible depression of baseline responding was observed in sessions which followed the ECS. The number of responses emitted in these sessions decreased and the variability of the rate of responding increased. A similar baseline depression was seen when a strong nonconvulsive shock or an injection of the drug acetoxycycloheximide was given immediately after a baseline session. Baseline depression was attributed to the ability of ECS to act as an aversive stimulus. This interpretation is discussed in relation to the effect of ECS on con-

ditioned suppression in the first set and to other investigations of the stimulus properties of amnesic agents. The importance of stimulus properties in the design and interpretation of experiments dealing with retrograde amnesia is also discussed. (Journal abstract modified)

110922 Fibiger, Hans Christian. Princeton University A biphasic action of pilocarpine on behavioral arousal in the rat. (Ph.D.dissertation). ***Dissertation Abstracts International.*** **Ann Arbor, Mich., Univ.M-films, No.71-1595 HC$10.00 MF$4.00 47 p.**

The effect of the cholinomimetic, pilocarpine, on behavioral arousal as measured by locomotor activity was investigated in the rat. Pilocarpine first produced a period of behavioral inhibition, the intensity and duration of which was dose related. After the inhibitory phase, a period of marked psychomotor excitation was observed. Pretreatment with scopolamine prevented both the inhibitory and excitatory effects of pilocarpine. Scopolamine administered at the onset of the rebound period however, significantly potentiated this excitatory phase. The anticholinesterase, physostigmine, also had a biphasic effect on behavioral arousal. The results are interpreted as indicating central adrenergic induction in response to central cholinergic stimulation. (Journal abstract modified)

112003 Hecht, K.; Treptow, K. Institute of Cortico-Visceral Pathology and Therapy, German Academy of Sciences, Berlin-Buch, Germany A study of pharmaco-dynamics in periodic conditional processes in albino rats. ***Activitas Nervosa Superior (Praha).*** **13(2):92-95, 1971.**

The effect of different neuro- and psychotropic drugs on the periodic courses of reaction times of conditional locomotor avoidance reflexes in albino rats is reported. The effects of 10mg/kg caffeine, 10mg/kg ethyl-crotyl-barbiturate, 0.2and 0.5mg/kg chlorpromazine, subcutaneously injected, were examined. The drugs in the first phase decreased significant portions and wavelengths of reaction times and motor reactions times. In the second phase of action the frequency spectra had either comparatively large significant portions, indicating that the drug action was continuing, as with 0.2mg/kg chlorpromazine, or a tendency to drop back to the initial frequency as in caffeine and kalypnon. The large dose of chlorpromazine caused a considerable disturbing effect, culminating in the second experimental phase where hardly any periodicities could be observed. 12 references.

126051 Foldi, M.; Zoltan, O.T. 3380 Goslar, Marienbader Weg 31, Germany /Unconditioned reflex activity in the rat suffering from experimental lymphogenic encephalopathy and the therapeutic effect of coumarin from Melilotus officinalis./ Die unbedingte Reflextatigkeit bei der experimentellen lymphogenen Encephalopathie und deren therapeutische Beeinflussung durch Cumarin aus Melilotus officinalis. ***Arzneimittel-Forschung (Aulendorf).*** **20:1623-1624, 1970.**

A marked similarity can be detected between the behavior of normal rats treated with a tranquilizer and those suffering from experimental lymphostatic encephalopathy. Coumarin exerts a marked therapeutic action in restoring unconditioned reflex activity to normal. Unconditioned reflex activity in the rat suffering from experimental lymphogenic Encephalopathy and the therapeutic effect of coumarin was studied on the rat (Melilotus officinalis). 2 references. (Author abstract)

126052 Sonkodi, S. II. Medizinische Universitatsklinik, Szeged, Hungary /Decrease of spontaneous motility in experimental lymphogenic encephalopathy and the protective activity of coumarin from Melilotus officinalis./ Die Abnahme der spontanen Motilitat bei der experimentellen lymphogenen Encephalopathie und die protektive Wirkung des Cumarins aus Melilotus officinalis. ***Arzneimittel-Forschung (Aulendorf).*** **20:1617, 1970.**

Decrease of spontaneous motility in experimental lymphogenic encephalopathy and the protective activity of coumarin from rats (Melilotus officinalis) were studied. The block decreased the motility essentially. Therapy with coumarin reduced its influence by half. 14 references. (Author abstract)

126053 Foldi, M.; Zoltan, O.T. 3380 Goslar, Marienbader Weg 31, Germany /Effect of a deficiency of pantothenic acid and pyridoxine on the function of the central nervous system and its response to coumarin from Melilotus officinalis./ Die Wirkung eines Mangels an Pantothensaure und Pyridoxin auf die Funktion des Zentralnervensystems und dessen Beeinflussung durch Cumarin aus Melilotus officinalis. ***Arzneimittel-Forschung (Aulendorf).*** **20:1618-1619, 1970.**

The effect of a deficiency of pantothenic acid and pyridoxine on the function of the central nervous system and its response to coumarin was studied in the rat (Melilotus officinalis). It was confirmed and numerically defined that a defi-

ciency of pantothenic acid and pyridoxine reduces the activity of conditioned reflexes. Learning ability is diminished and behavior already acquired is forgotten again. The antivitamins used act by themselves and not as unspecific toxic substances. Their effect could be neutralized when they were administered in combination with vitamins. These data demonstrated the extensive connections between lymphogenic encephalopathy and a deficiency of pantothenic acid and pyridoxine. The possibility of neutralizing specific antipantothenic acid antipyridoxine effects by means of coumarin deserves special consideration. Thus coumarin acts under these conditions as if it belonged to the group of vitamins B. Moreover, experimental lymphogenic encephalopathy can be favorably influenced by therapy with coumarin. 6 references. (Author abstract modified)

126054 Foldi, M.; Zoltan, O.T. 3380 Goslar, Marienbader Weg 31, Germany /Effect of chlorpromazine on conditioned reflexes and antagonistic activity of coumarin from Melilotus officinalis./ Die Wirkung von Chlorpromazin auf die bedingte Reflextatigkeit und die antagonistische Wirkung von Cumarin aus Melilotus officinalis. *Arzneimittel-Forschung (Aulendorf).* 20:1619-1620, 1970.

The decrease of conditioned reflexes in the rat characteristic for the action of chlorpromazine is antagonized by coumarin and by panthenol and pyridoxine. The effect of chlorpromazine (10-(gamma-dimethylaminopropyl)-2-chlorophenothiazine) on the conditioned reflexes and antagonistic activity of coumarin was studied in the rat (Melilotus officinalis). 4 references. (Author abstract)

126055 Foldi, M.; Zoltan, O.T.; Maurer, Maria. 3380 Goslar, Marienbader Weg 31, Germany /Influence of isoniazid on the central nervous system; the antagonism between isoniazid and pyridoxine, pantothenic acid and coumarin in rats (Melilotus officinalis)./ Die Wirkung von Isonicotinsaurehydrazid (INH) auf das Zentralnervensystem und der Antagonismus zwischen dieser Substanz und Pyridoxin, Pantotensaure sowie Cumarin aus Melilotus officinalis bei Ratten. *Arzneimittel-Forschung (Aulendorf).* 20:1620-1623, 1970.

The influence of isoniazid on the central nervous system and the antagonism between isoniazid and pyridoxine, pantothenic acid and coumarin was studied in rats (Melilotus officinalis). A marked deterioration of conditioned reflex activity results in consequence of the administration of isoniazid in a subconvulsive dosage. This effect can be antagonized by pyridoxine, by pantothenic acid, and by coumarin. The effect of a convulsive dosage of isoniazid can be antagonized by coumarin. 1 reference. (Author abstract)

126056 Foldi, M.; Zoltan, O.T. 3380 Goslar, Marienbader Weg 31, Germany /Learning ability in experimental lymphogenic encephalopathy under the influence of coumarin from Melilotus officinalis./ Das Lernvermogen bei der experimentellen lymphogenen Encephalopathie unter dem Einfluss von Cumarin aus Melilotus officinalis. *Arzneimittel-Forschung (Aulendorf).* 20:1614-1616, 1970.

The learning ability of rats (Melilotus officinalis) in experimental lymphogenic encephalopathy under the influence of coumarin was studied. The learning ability of rats is reduced in lymphogenic encephalopathy. The fact that the animals afflicted gradually recover their learning ability after one week could be explained mainly by a spontaneous healing process of the encephalopathy by regeneration of the lymph vessels. By a cervical lymphangio -thrombophlebitis the learning ability of the rat was likewise diminished to a statistically significant degree. It should be emphasized that the effect of a cervical venostasis does not differ from that of a sham operation. It would be mistaken to explain the effect of a cervical lymph block by the erroneous assumption that the lymphedema of the neck induced by mechanical insufficiency of the cervical lymph flow caused secondarily a cervical venostasis and that encephalopathy was the consequence of the venostasis. It is confirmed that the favorable influence of coumarin on the impeded function of the central nervous system in lymphogenic encephalopathy is caused either by a cervical lymph block or by a cervical lymphagio - thrombophlebitis. The learning ability of coumarin treated animals suffering from a cervical lymph block does not differ from that of animals having undergone a sham operation. 2 references. (Author abstract)

05 TOXICOLOGY AND SIDE EFFECTS

103004 Nix, Charles Ray. University of Mississippi Studies of the toxic effects of drugs on electrical conduction and function of the heart.

(Ph.D.dissertation). *Dissertation Abstracts International.* Ann Arbor, Mich., Univ.M-films, No.71-10235, HC$10.00 MF$4.00 99p.

The toxic effects of drugs on electrical conduction and function of the rabbit heart was studied. A positive inotropic effect is exerted on stimulated left atria of rabbits by the Erythophleum alkaloid cassaine, and its methiodide and ethiodide. The minimal concentration of cassaine which will augment contractility, as well as the 2 alkylated derivatives, are noted. Also, the cardiotoxic effects of high concentrations imipramine and 4 psychotoxic phenylethylamine derivatives on the isolated perfused heart of the rabbit were examined. Mescaline, methylenedioxyamphetamine, and imipramine produced both negative inotropic and chronotropic effects. Amphetamine and methamphetamine produced augmentation of contraction in some preparations, although negative inotropic effects were observed in time. Furthermore, in all hearts which were treated with amphetamine and methamphetamine an initial acceleration, and later a diminution in rate of contraction was noted. Electrical tracings were also obtained from the isolated heart experiments. Such toxic manifestations as atrioventricular block, ectopic ventricular activity and interventricular conduction disturbances were observed. (Journal abstract modified)

105619 Sommer, H.; Quandt, J. Bezirkskrankenhaus, 435 Bernburg, Germany /Long-term treatment with chlorpromazine in animal experimentation./ Langzeitbehandlung mit Chlorpromazin im Tierexperiment. *Fortschritte der Neurologie, Psychiatrie und ihrer Grenzgebiete.* 38(9):466-491, 1970.

The testing of drugs in animals by the determination of the toxicity threshold may not be totally justified as is indicated by the pathological anatomic examination of the experimental animal. Long-term experiments in animals are considered to be mandatory. Chlorpromazine (Megaphen) was administered orally to rabbits daily over a period of 6 mos. The animals were divided into 5 groups of 4 and 1 control group of 2 animals, and the oral dose was administered daily in amounts of 3.3, 6.7, 10, 13.3and 16.7mg/kg. The animals receiving the 16.7mg/kg dose survived the period of experimentation, but died within 14 days following the discontinuation of the drug. The histological and histochemical analysis showed increased brain damage with increasing doses. There was clear evidence of gliosis among the various forms of nerve cell damage. Further, depending on the dosage level, carbohydrate metabolic disturbance was evident, particularly in the limbic system, which is an expression of an irreversible redox system blockage. In view of its wide use in psychotherapy, it is vital to take into consideration the effects of chlorpromazine over a long period of time. 112 references. (Author abstract modified)

106778 Gotfredsen, C.F.; Rafnelsen, O.J. Psychochemistry Institute, University Department of Psychiatry, Rigshospitalet, 9, Blegdamsvej, DK-2100 Copenhagen, Denmark Effects of lithium and other psychopharmaca on rat electrolyte metabolism. *International Pharmacopsychiatry (Basel).* 5(2-4):242-248, 1970.

The effect of lithium chloride, chlorpromazine, imipramine, and reserpine on electrolyte metabolism in rats was studied. It was found that these drugs influenced the urinary excretion of calcium and phosphate in different ways. During isotope studies with calcium and phosphate, lithium, chlorpromazine, and imipramine changed the incorporation of calcium and/or phosphate into diaphragm. The most pronounced change observed was the doubling of phosphate incorporation into muscle after lithium. 17 references. (Journal abstract modified)

106779 Thomsen, K. Psychopharmacology Research Unit, Aarhus University Psychiatric Institute, 8240 Risskov, Denmark Lithium-induced polyuria in rats. *International Pharmacopsychiatry(Basel).* 5(2-4):233-241, 1970.

Rats given lithium with the fodder in a dosage of about 1mEq/day/kg body weight developed a pronounced polyuria, which remained stable for months. The serum lithium concentration remained around 0.7mEq/l, and the animals were, apart from reduced weight gain, unaffected by the treatment. The polyuria did not respond to the administration of vasopressin: it was accordingly of renal and not of pituitary origin. Small changes in serum and tissue electrolytes were presumably secondary to the increased urine flow. Creatinine and lithium clearances were unchanged. The lithium induced polyuria was fully reversible; after discontinuation of lithium, urine flows fell to normal values within 5-8 days. Administration of lithium in a higher dosage (about 1.5mE/q/day/kg) also led to the development of polyuria, but after

a few weeks the condition became unstable. The urine flow started to fall, and serum lithium, which had been around 1.1mEq/l, started to rise. On continued lithium administration the rats would eventually die, but on discontinuation the condition was fully reversible until shortly before death. 16 references.(Journal abstract)

114837 Masuda, Hiroshi; Nishiyama, Takao; Matsunuma, Naochika; Kimura, Kunio; Okonogi, Takashi; Suzuki, Yoshio. Research Laboratories Sankyo Co., Ltd., Tokyo, Japan The safety test of L-Dopa. I.Acute and subacute toxicity of L-DOPA in experimental animals. *Annual Report of Sankyo Research Laboratories (Tokyo).* 22:142-164, 1970.

A report on the acute and subacute toxicity of L-Dopa is presented, based on oral, intraperitoneal, subcutaneous and intravenous administration in mice and rats. L-Dopa orally (10mg/kg) and intravenously (2.5mg/kg) administered in beagle dogs causes vomiting and salivation, but no toxic indications are observed in dogs during and after intravenous administration at dosages of 12.5, 7.5and 2.5mg/kg/day for 97 days. L-dopa orally administered in rats for five weeks does not cause any toxic responses at dosages under 400mg/kg/day; however, it diminishes body weight at dosages of 800 and 1000mg/kg/day. No toxic effects are observed in rats which ar e intraperitoneally administered at dosages of less than 200mg/kg/day for five weeks. 6 references. (Author abstract modified)

06 METHODS DEVELOPMENT

102415 Strada, Samuel Joseph. Vanderbilt University Adrenergic mechanisms in the central action of psychotropic drugs. (Ph.D.dissertation). *Dissertation Abstracts International.* Ann Arbor, Mich., Univ.M-films, No.71-10466, HC$10.00 MF$4.00 156 p.

An attempt was made to determine whether the push - pull cannula technique, as a means of investigating release mechanisms in the central nervous system, could furnish information on drug induced changes in the availability of adrenergic neurohumors at central adrenergic effector sites. Also studied was whether the push - pull cannula technique could furnish information on drug induced changes in the availability of norepinephrine at central adrenergic effector sites. It was shown that conclusions on the actual availability of norepinephrine at central effector sites could be drawn from the analytical data obtained. These results are described in detail. The results obtained with the push - pull cannula support the view that the action of p-chloroamphetamine is predominantly mediated through the release of stored catecholamines, whereas the central stimulatory action of amphetamine does not depend on stored norepinephrine as long as the synthesis of the catecholamines is maintained. (Journal abstract modified)

105622 Schelkunov, E.L. Laboratoriya Psikhofamakologii Leningradskogo Nauchno-Issledovatel'skogo Psikhonevrologicheskogo Instituta IM.V. M.Bekhtereva, Leningrad /5-hydroxytryptophan-produced hypothermia in mice as a test for pharmacological differentiation of antidepressants, anticholinergics and neuroleptics: some data on the nature of this hypothermia./ 5-oksitriptofanovaya gipotermiya kak test dlya razeranicheniya antidepressantov, kholinolitikov i neyroleptikov i nekotoryye dannyyeo prirode etoy gipotermii. *In: Lapin, I., Serotoninergic processes in the action of psych.drugs.* Leningrad, RSFSR Ministry of Health, 1970. 237 p. v.53 (p.150-176).

Tricyclic antidepressants (imipramine, DMI, nortriptyline) in minimal doses tested (2mg/kg and more) conteract hypothermia in mice produced by administration of 5-HTP in doses of 250 to 300mg/kg. Some anticholinergics (benactyzine, scopolamine) also diminish 5-HTP hypothermia in doses higher than 50mg/kg. Propionylic derivatives of 2-chlorphenothiazine (chloracizine, L-III) counteract 5-HTP hypothermia in doses of 10mg/kg and more. Neuroleptics enhance the hypothermic effect of 5-HTP. Doses of antidepressants and anticholinergics which counteract hypothermia in mice produced by intraperitoneal injection of L-dopa (200mg/kg) do not differ from each other. Thus, 5-HTP hypothermia in mice may be utilized (in contrast to dopa produced hypo- thermia) for pharmacological differentiation antidepressants both from anticholinergics and neuroleptics. Analysis of 5-HTP hypothermia which included the study of hypothermic effect of intraperitoneally injected serotonin, administration of serotonin and 5-HTP decarboxylase (NSD-1024), and also of quaternary derivatives (methyl iodides) of imipramine and chloracizine, not penetrating into the brain, give rise to the idea that hypothermia in mice by intraperitoneal adminis- tration of 5-HTP is caused

by serotonin formed from 5-HTP in the brain. The high degree of effectiveness of antidepressants in counteracting 5-HTP hypothermia is a result of their inhibitory action on the pro- cess of transport of 5-HTP into the brain neurones, resulting in the diminution of the quantity of serotonin formed in the brain from 5-HTP. 27 references. (Author abstract modified)

131625 Nanikawa, Ryo; Kotoku, Susumu; Sumida, Yasuteru. Department of Legal Medicine, Tottori University School of Medicine, Yonago, Japan Separation and identification of tranquilizers and psychostimulants. ***The Japanese Journal of Legal Medicine (Tokyo).*** **24(4):326-330, 1970.**

The use of gas chromatography in the separation and identification of tranquilizers and psychostimulants is described. Thirty eight kinds of drugs available on the Japanese market were individually examined. The chromatography column was 2m in length and 0.3cm in diameter. The column packing consisted of 0.5% SE-30 on chromosorb W (60-80 mesh) under temperatures of 150-250 degrees Centigrade and used nitrogen at 45ml/min pressure as the gas carrier. The various drugs were identified by a hydrogen flame ionization dector. Most of the 38 drugs were dectable by gas chromatography. The drugs which had a hydroxy radical in their molecular structure were detected only after methylation. (Author abstract modified)

07 EARLY CLINICAL DRUG TRIALS

100959 Turner, M.; Cordero Funes, J.R.; Aspinwall, R.; Cantlon, B.; Fejerman, N.; Lon, J.C. author address not given /Clinicoelectroencephalographic evaluation of a new benzodiazepinic derivative (Ro 05-4023) administered orally in epileptic patients using a double blind method./ Ensayo de valoracion clinicoelectroencefalografica de un nuevo derivado benzodiazepinico (Ro 05-4023) por administracion oral en pacientes epilepticos con tecnica de doble ceguera. *Acta Neurologica Latinoamericana (Montevideo).* 16(1-4):158-169, 1970.

A therapeutical test using the double blind method was conducted in conjunction with a group of 18 epileptic children (8 absences, 6 Lennox-Gastaut syndrome and 4 West syndrome), using a new diazepinic derivative, Ro 05-4023, and a placebo, given orally. Doses were in the neighborhood of 3mg for children under 3 years and from 4 to 6mg for older children. The clinical and electroencephalographic changes produced over several months of trial (average of 5 months) with drug and placebo in the same cases showed a statistically significant difference in favor of the active drug, Ro 05-4023. This experience confirms the assumptions advanced in a previous report using intravenous injection of the drug controlled by electroencephalographic observation of the efficacy of this new diazepinic derivative for the inhibition of paroxystic electroencephalographic and clinical discharges. These properties render it highly suitable for treatment of epileptics with frequent fits and unamenable to classical anticonvulsive therapy (absences and epileptogenic encephalopathies in children). 5 references. (Journal abstract modified).

101034 Vencovsky, E.; Peterova, E.; Baudis, P. Psychiatrische Klinik der Karlsuniversitat, Pilsen, Czechoslovakia /Clinical testing with fluphenazine depot administration to schizophrenic patients./ Klinische Erfahrungen mit der Applikation von Fluphenazin-Depot bei Schizophrenen Kranken. *Psihofarmakologija 2: Radovi Drugog Jugosl.Phihof.Simpozija -- 1969.* Zagreb, Medicenska Naklada, 1970. 441 p. (p.285-288).

The effect of long-term therapy with injections of fluphenazine (Lyogen depot) in 28 patients (12 Males, 16 females) with psychoses related to schizophrenia, is described. The analysis revealed that improvement with this therapy is more marked in those patients who responded favorably to other psychopharmaceuticals, or who manifested complete disappearance of psychotic symptoms. The longest remissions lasted for 9 mon, and with long-term lyogen depot treatment, remissions were observed in the markedly improved patients. Relapses occurred mostly during the first month of treatment, and were manifested by a worsening of the most outstanding psychotic symptoms; but in 6 patients, a depressive symptomatology with suicidal tendencies was noted. Extra- pyramidal symptomatology was seen in 10 patients, oculogyria in 1, and oral dyskinesia in another patient. The rest showed signs of tremor, rigor or acathisia. In 8 patients given antiparkinson medication, no extrapyramidal symptoms appeared. An advantage of this therapy is that it is preferred by patients as compared to the daily oral admin- istration in the form of pills. 4 references.

105486 Turner, M.; Fejerman, N.; Schugurensky, E.; Cordero Funes, J.R.; Cantlon, B.; Aspinwall, R.; Lon, J.C. author address not given /Clinicoelectroencephalographic evaluation of the antiepileptic action of a new series of benzodiazepinic derivatives./ Evaluacion clinicoelectroencefalografica de la accion antiepileptica de una nueva serie de derivados benzodiazepinicos. *Acta Neurologica Latinoamericana (Montevideo).* 16(1-4):97-109, 1970.

The effects of 2 benzodiazepinic derivatives, Ro 4-5360 (Mogadan) and Ro 5-4023, were assessed in 50 epileptics with very frequent clinical seizures and paroxsmalhypersynchronic electroencephalogram (EEG) discharges by slow intravenous injection under EEG control, and later by chronic oral administration. Doses ranged from 2 to 10mg for Mogadan and from 0.5to 1mg for Ro 5-4023. Effective results were obtained in 30 cases, with complete suppression of the discharges and normalization of the EEG. In 5 cases, effective results were obtained by decreasing the number of paroxysmal discharges. In 15 cases, no modification of the EEG was observed. A statistical correlation analysis showed that Ro 4-5360 was more effective than Ro 5-4023 in suppressing the pathological EEG discharges in the

epileptogenic encephalopathy. Of 11 cases which received the drugs orally, 7 showed suppression of seizures, 3 reduction of seizures, and 1 no effect. 16 references.

105730 Gross, H.; Haberler, H. II.Psychiatrische Abteilung des Psychiatrischen Krankenhauses der Stadt Wien, Vienna, Austria /Clinical experience with methylperone (Buronil), a new butyrophenone derivative./ Klinische Erfahrungen mit Methylperon (Buronil), einem neeun Butyrophenonderivat. ***International Pharmacopsychiatry (Basel).*** **5(1):44-53, 1970.**

Methylperone, a new major tranquilizer of the benzophenone series and with a moderately broad therapeutic spectrum, presents a good antipsychotic effect, especially on acute exacerbations and cases of schizophrenia of recent onset. Oral and parenteral therapy are of equal value, so that the former is preferable on account of the fewer side effects. Marked sedation is obtained only with high doses. The main side effects consist of hyperkinetic and hypertonic parkinsonian symptoms, which are easily controlled by the usual antiparkinson remedies. The latter should also be given by mouth, because of the danger of drug induced delirium. Experience with 104 male schizophrenics in the psychiatric hospital in Vienna has shown that methylperone, after initial treatment in hospital and appropriate adjustment of the dosage, is most suitable for continued use on an outpatient basis and for long-term therapy. 19 references. (Author abstract modified)

114835 Takagi, Hiromu; Kamioka, Toshiharu; Kobayashi, Shinsaku; Kumakura, Seiji; Oshima, Takeshi; Nakayama, Koichi. Research Laboratories Sankyo Co., Ltd., Tokyo, Japan Pharmacological studies of oxazolazepam, a new psychotropic agent -- II, general pharmacology and subacute toxicity. ***Annual Report of Sankyo Research Laboratories (Tokyo).*** **22:286, 1970.**

A report on the general pharmacological effects and subacute toxicity of oxazolazepam, a new psychotropic agent, is presented, in comparison with that of chlordiazepoxide. The results show: oxazolazepam causes slight hypotension and depression of heart rate in larger doses but no significant effects on respiration, ECG and responses to autonomic drugs: the hypotension and depression of heart rate are weaker than those effects induced by chlordiazepoxide. Other effects, such as miosis, hypothermia, constipation and physical dependence are less demonstrated by oxazolazepam than by chlordiazepoxide; emetic, antiinflammatory and diuretic actions are not observed in the effects of these drugs. The subacute toxicity of oxazolazepam is definitely less than that of chlordiazepoxide. (Author abstract modified)

129367 Hasegawa, Kazuo; Yamada, Osamu. Department of Neuro-psychiatry, Tokyo Jikei University, School of Medicine, Tokyo, Japan A clinical experience of Oxazolam, a new minor tranquilizer. ***Clinical Psychiatry (Tokyo).*** **12(7):613-622, 1970.**

A report on the effect of Oxazolam, a new minor tranquilizer, is presented, based on clinical experience of administrating the drug through oral dosages ranging from 30 to 60mg a day. The drug was given to 15 patients with anxiety psychosis, 15 patients with light depression, and eight patients with other mental problems. Results show the drug was effective in 28 cases and non effective in 10. The drug was most effective in cases of anxiety psychosis, with an efficiency rate of 86.7% and somewhat effective in cases of light depression, efficiency rate of 60%. A side-effect of sleepiness was observed, but the symptoms were not serious.

129879 Maeda, Toshio. Niigata Mental Hospital, Japan Clinical application of new tranquilizer, CS-300, to schizophrenics. ***Clinical Psychiatry (Tokyo).*** **12(5):431-442, 1970.**

A report on the effect of CS-300, a new minor tranquilizer, on schizophrenia and epilepsy is presented, based on the clinical administration of the drug through daily oral dosages averaging 30mg during a two month period to 30 schizophrenics, 13 epileptics, and 7 patients with neurosis who were hospitalized at Niigata Mental Hospital and had not shown any improvement under other minor tranquilizers. The results show that CS-300 is effective for 52% of the schizophrenics. The effect of the drug on schizophrenia is considered to be due to its stabilization action on emotion. No side effects such as sleepiness, relaxation of muscle, fatigue which are often induced by Diazepam were found in CS-300 and the drug is effective for all the patients with neurosis, and for 62% of the epileptic patients. Therefore the drug was effective for 64% of all the patients studied. 9 references.

08 DRUG TRIALS IN SCHIZOPHRENIA

101681 Becker, Robert E. Department of Psychiatry, University of Connecticut Health Center, 2 Holcomb Street, Hartford, Conn. 06112 Evaluation of an amitriptyline-perphenazine combination in chronic schizophrenia. *American Journal of Psychiatry.* 127(6):827-831, 1970.

A controlled study is described of an amitriptyline and perphenazine combination given to 58 chronic schizophrenic patients. There was no evidence of the combination's increased effectiveness over perphenazine used alone. The possibility of therapeutic incompatibility between perphenazine and amitriptyline at some dosage levels is discussed, and it is concluded that evidence does not support using a perphenazine and amitriptyline combination. 27 references.(Journal abstract modified)

103255 Goldstein, Michael J. Department of Psychology, University of California at Los Angeles, Los Angeles, California Premorbid adjustment, paranoid status, and patterns of response to phenothiazine in acute schizophrenia. *Schizophrenia Bulletin.* No.3(Winter):24-37, 1970.

It is suggested that a particular phenothiazine interacts with a schizophrenic patient's lifelong pattern of, and effectiveness in, coping with stress. Schizophrenics with good premorbid histories may be paranoid or nonparanoid, but those with poor premorbid histories are usually nonparanoid. Poor premorbid patients respond to drug or placebo treatment according to clinical expectation, but good premorbid patients respond in a reverse pattern. Among good premorbid patients, paranoids on placebo show decreased cognitive adequacy and greater vigilance for environmental threat (a behavior pattern far less apparent with active medication), and nonparanoids show no deterioration on placebo and little positive drug response (suggesting an adverse affect by phenothiazine treatment). 13 references.(Author abstract modified)

103273 Rice, Marc. Yeshiva University A psychological study of the effects of chlorpromazine (Thorazine). (Ph.D.dissertation). *Dissertation Abstracts International.* Ann Arbor, Mich., Univ.Mfilms, No.71-14297 HC$10.00 MF$4.00 87 p.

A theory is presented which holds that chlorpromazine has no effect on schizophrenia but induces a state of overriding depression that suppresses or masks the expressive and behavioral aspects of the psychosis. The diminution of behavioral psychotic signs is not, in general, reflected in measures of perception or ideation. Rather the psychosis remains largely unaffected. A study was organized to test the theory. Ten schizophrenic patients were chosen according to specific psychiatric criteria and tested on the Holtzman Inkblot Test in the predrug period and again in the postdrug period. Each patient was his own control with the primary data in the form of difference scores. Each patient was given a drug course adequate to controlling his individual symptomatology. Six drug free patients formed the control group. The findings tend to statistically support the theoretical position. (Journal abstract modified)

105623 Cazzullo, C.L.; Cocchi, A.; Fonda, P.; Goldwurm, G.F. Institut de la clinique psychiatrique de l'universite de Milan, Italy /Psychodynamics of the response to pharmacologic treatment with neuroleptics in schizophrenics./ Psychodynamique de la reponse au traitement pharmacologique avec neuroleptiques dans les schizophrenes. *Psihofarmakologija 2: Radovi Drugog Jugosl.Psihof.Simpozija -- 1969.* Zagreb, Medicenska Naklada, 1970. 441 p. (p.107-111).

The action of neuroleptic drugs in the treatment of mental patients may not only be related to the pharmacodynamic properties of these drugs, but also to the rapport established by the patient with the drug, which may afford him the means of establishing contact with society. The psychodynamics of the patient's reactions involve, aside from the drug, his hospital surroundings and his physician. The drug - patient relationship was investigated in a group of 50 schizophrenics (ages 18 to 55 years) by means of a questionnaire. Although 80% ac- knowledged their illness, only 33% admitted having a mental disorder; the others claimed that their illness was organic. Although 55% of the patients would not accept the psychic nature of their disorders, they reported that the drug had an effect on their psychic state. Some 30% of the Ss indicated their fear of personality damage by the medication. In some cases refusal to take the emdication by the patients who have improved may be due to their association of the drug with their previous image of themselves. The patient -drug relationship represents a very important element in the study of the mental patient. 11 references.

109788 Izakson, Kh.A. author address not given /Concerning the article by N.N.Timofeyev, V.T.Kondrashenko and N.Y.Nemtseva on 'Oxymetric Investigation of Patients with Schizophrenia and Reactive Psychosis During Neuroleptic Treatment.'/ Po povodu stat'i N.N.Timofeyeva, V.T.Kondrashenko, N.Ya. Nemtsevoy 'Oksigemometricheskiye issled.bol'nykh shizofreniyey i reaktivnym psikhozom v protsesse lecheniya ikh neyroleptikami.' *Zhurnal nevropatologii i psikhiatrii imeni S.S.Korsakova (Moskva).* 70(7);1103-1104, 1970.

A critical evaluation is given of an article on neuroleptic treatment of patients with schizophrenia and reactive psychosis. It is noted that inadequate procedures and calculation in the original investigation to determine minimum respiratory volume led to inaccurate conclusions. Literature is cited in which may be found a simple formula for calculation of the correct minute volume of respiration. It is suggested that the original results would have been more correct than the average abstract figures given if the figures of minute respiratory volume had been expressed in percentages of correct values. It is also pointed out that oxymetry, which determines only the final results of blood oxygenation in the lungs, cannot in itself resolve the problem of the cause of hypoxemia. For this reason, the data obtained should be compared to clinical data and spirographic indicators to avoid error. 6 references.

111022 Sokolova, Ye.D. Institut psikhiatrii AMN SSSR, Moscow /Experimental use of preparation Luvatren in schizophrenic patients./ Opyt primeneniya preparata 'luvatren' u bol'nykh shizofreniyey. *In: Shternberg, E., Problemy organizatsii psikhiatri.pomoshchi kliniki.* Moscow, Sovetskaya Rossiya, 1970. 130 p.(p.97-100), Part 1.

Luvatren (methyl peridol, R), a derivative of butyrophenone, was used to treat 36 patients with schizophrenia. The patients were divided into 2 groups according to the age at which the schizophrenia began. In the first group the best results of treatment were noted in patients with paroxysmal course of paranoid schizophrenia. The drug was less effective in treating patients with a continuous course of paranoid schizophrenia. Luvatren was effective in treating cases of early schizophrenia with a torpid course, psychopathic-like symptoms and individual hypochondriacal delirious ideas. The experiments show that the drug is easily tolerated and is of low toxicity. Comparison of the effects of Luvatren and haloperidol shows that the former is more effective in treating paranoid schizophrenia with a paroxysmal course.

111031 Kozyrev, V.N.; Belyy, B.I.; Zarochintseva, A.V.; Belaya, I.I.; Kozyreva, S.Ye.; Pakhter, A.Sh.; Rozhin, V.M. Dmitrovskaya psikhiatricheskaya bol'nitsa No.9 Moskovskoy oblasti, Dmitrov, USSR /Use of neuleptil in treatment of patients with schizophrenia./ Primeneniye neyleptila pri lechenii bol'nykh shizofreniyey. *In: Shternberg, E., Problemy organizatsii psikhiatri.pomoshchi kliniki.* Moscow, Sovetskaya Rossiya, 1970. 130 p.(56-59), Part 1.

Neuleptil was used in capsules (10mg of the drug per capsule) or in drops (lmg of the drug per drop) to treat 56 patients with schizophrenia, who ranged in age from 20 to 59 years and had a history of illness from 1 year to more than 10 years. The effects of the drug were usually manifested over a course of the first 5 or 10 days. Significant therapeutic effect or an improvement of the course of the disease was achieved in 65% of the cases, the remainder being unchanged. It is noted that, besides the positive effect in various psychopathic-like disorders, neuleptil has an antipsychotic effect which is manifested mainly in those psychopathological symptoms where affective disorders occupy a significant position. The favorable results of using neuleptil in some cases of persistent verbal hallucinosis are indicated.

111032 Kagan, I.S. Moskovskaya psikhiatricheskaya klinicheskaya bol'nitsa No.1 im. Kashchenko, Moscow /On the problem of treatment and some clinical characteristics of schizophrenia with a gradual paroxysmal-like course./ K voprosu o terapii i nekotorykh klinicheskikh osobennostyakh shizofrenii s pristupoobrazno-progrediyentnym techeniyem. *In: Shternberg, E., Problemy organizatsii psikhiatri.pomoshchi kliniki.* Moscow, Sovetskaya Rossiya, 1970.130 p.(p.51-55), Part 1.

The clinical characteristics and course of psychosis in the group of paroxysmal schizophrenia and the effect of treatment with psychotropic drugs on the course and clinical manifestations of the disease were studied in 100 patients ranging in age from 25 to 60 years. The patients were divided into 3 clinical groups, the first group being distinguished by a paroxysmal-like course of the disease, but similar to paranoid schizophrenia in its clinical manifestations; the

second group distinguished by acute polymorphous seizures; and the third group in which aggravations of the affective - delirious seizure type were noted on a background of a torpid course. Administration of psychotropic agents in various combinations war effective in varying degrees in achieving remissions. Clinical analysis within the framework of the isolated groups permits substantiation of treatment of selection with consideration of both the psychopathological characteristics and the stage of the course of the disease. Correct and timely selection of the nature and structure of maintenance treatment, as as of methods of work and social rehabilitation and readaptation.

111034 Zavidovskaya, G.I.; Matveyeva, Ye.S.; Rumyantseva, G.M. Institut psikhiatrii AMN SSSR, Moscow /On the problem of ambulatory treatment of schizophrenia with psychotropic drugs./ K voprosu ob ambulatornoy terapii shizofrenii psikhotropnymi sredstvami. *In: Shternberg, E., Problemy organizatsii psikhiatri.pomoshchi kliniki.* Moscow, Sovetskaya Rossiya, 1970.130 p.(p.41-47), Part 1.

Some characteristics of treating 70 patients with schizophrenia, using several psychotropic drugs with different effects (tranquilizers, neuroleptics and antidepressants) are considered. The observations showed that combined therapy should be the main method of treating schizophrenia characterized by a low gradient and polymorphism of clinical manifestations, made up of affective, neurosis-like and rudimentary delirious disorders. Combined treatment should include simultaneous use of neuroleptic drugs, tranquilizers and antidepressants. The different combinations of drug for various schizophrenic and epileptic states are indicated.

114885 Colucci d'Amato, F. Ospedale Psichiatrico Provinciale 'L.Bianchi', Naples, Italy /Chemical and clinical evaluation of the use of Gabob in schizophrenic patients./ Valutazione chimico-clinica dell'uso del Gabob in pazienti schizofrenici. *Ospedale Psichiatrico (Napoli).* 38(3):377-382, 1970.

After two months of treatment with Gaba, in daily doses of 500mg to 4g, eight of nine women with schizophrenia simplex and three of seven with hebephrenic schizophrenia presented improvement consisting of reduction of impulsion, increase of self-control, thinking ability and will. While treatment with Gaba did not produce such improvement in four patients with paranoid schizophrenia, all these patients presented improvement of self-control and thinking after six months of therapy with the compound. After six months of treatment, all the patients with schizophrenia simplex and five of seven with hebephrenic schizophrenia exhibited improvement. There were no instances of side-effects. 10 references.

115037 Merlis, S.; Sheppard, C.; Fracchia, J.; Collings, L. Clinical and Research Facilities, Research Division, Central Islip State Hospital, Central Islip, NY Influences of polypharmacy on hallucinatory behavior in a sample of female chronic schizophrenic patients. *In: Keup, W., Origin and mechanisms of hallucinations.* New York, Plenum Press, 1970.479 p.(p.465-470).

Some influences are reported of polypharmacy (the practice of prescribing two or more psychoactive medications to one patient for the purpose of reducing or controlling psychiatric symptoms) on the hallucinatory behavior in a sample of female chronic schizophrenic patients. The results indicate that in the absence of psychoactive medications and following placebo therapy, hallucinatory behavior and overall pathology will increase within a 30 day period, and that two or more psychoactive medications add little benefit over single treatment forms.

116482 Dobrzanski, Tadeusz; Cianciara, Janusz. Internal Diseases Dept.for Nervous and Mental Patients, J.Mazurkiewicz State Hospital, Pruszkow, Poland Coexistence of diabetes mellitus and myxedema in mental patients. *Polish Endocrinology (Warszawa).* 21(1):40-43, 1970.

The rare coexistence of diabetes mellitus and myxedema is reported in six female patients with schizophrenia. Treatment with substitutive thyroid drugs did not exacerbate the course of diabetes, and regression of symptoms of myxedema was accompanied by improvement of the mental state of the patients. 16 references. (Author abstract modified)

118583 Takahashi, Saburo; Ito, Kozo; Suwa, Nozomi; Kato, Iwao; Watanabe, Hiroshi; Watanabe, Eiichi. Department of Psychiatry and Neurology, Hokkaido University School of Medicine, Japan A double-blind, cross-over comparison of APY-606 with chlorpromazine in chronic schizophrenia. *Clinical Psychiatry (Tokyo).* 12(5):421-427, 1970.

A double-blind, crossover comparison of APY-606 with chlorpromazine (CP) was studied in 30 chronic schizophrenic inpatients who had been treated by chlorpromazine (CP) for four to 26 years. One group of patients was given CP for the first eight weeks, APY-606 for the next eight weeks and CP for the following month. Another group was given APY-606 for the first eight weeks, CP for the next eight weeks, and CP again for the following month. The results were evaluated by psychiatrists and nurses. The psychiatrists judged APY-606 to be more effective than CP in four cases, less effective than CP in eight cases, and is the same as CP in 17 cases, indicating that CP was slightly superior to APY-606. The nurses judged the same amount of APY-606 to be less effective than the same amount of CP. 6 references.

123373 Wasik, August; Horodnicki, Jan; Sidorowicz, Slawomir. Klinika Psychiatryczna AM, ul.Kraszewskiego 25, Wroclaw, Poland /Administration of a new butyrophenone derivative, pimozide, in the treatment of schizophrenia./ Zastosowanie nowej pochodnej butyrofenonu -- pimozydu w leczeniu schizofrenii. *Psychiatri Polska (Warszawa).* 4(6):643-647, 1970.

The clinical efficacy of pimozide, a new butyrophenone derivative, was evaluated during its administration to 18 patients suffering from various forms of schizophrenia with a chronic course. In an average daily dose of 22mg over a minimum period of 20 days, pimozide improved the mental state of eight patients. The drug was found to be the most effective in hallucinatory delusional syndromes, but it had little influence in the sphere of effect. No serious side effects were observed. The drug is well tolerated by the vegetative and extrapyramidal systems and by the parenchymatous organs. It appears that the drug may be used in the treatment of chronic schizophrenic patients who are employed in workshops. 7 references. (Author abstract)

124309 Ridolo, P.; Tridenti, A. Istituto di Psiachiatria, Universita de Parma, Parma, Italy /Pigmentary retinopathy and paranoic syndrome. (Presentation of one case)./ Retinopatia pigmentosa e sindrome paranoidea (Osservazioni su di un caso). *Riv.Sper.di Fren.e Med.Legale delle Alienazione Ment. (Reggio Emilia).* 94(6):1580-1592, 1970.

The case of a 35-year-old female with pigmentary retinopathy and paranoid schizophrenia is described. The same conditions were manifested separately in some of her relatives, including a father with hallucinatory delirium. Administration of unspecified doses of clopenhixol induced objective improvement for a few months but the patient relapsed upon the arbitrary cessation of treatment. Subsequent hospitalization and treatment with levo-chlorpromazine resulted in disappearance of psychotic manifestations and resumption of critical ability but relapse occurred upon cessation of treatment. 7 references.

129082 Tanimukai, Hiroshi; Kaneko, Jiro. Department of Neuropsychiatry, Osaka University Medical School, Osaka, Japan A double-blind, controlled study of the effects of oxypertine and carpipramine on schizophrenia. *Clinical Psychiatry (Tokyo).* 12(1):55-64, 1970.

A report on the effect of oxypertine and carpipramine on schizophrenia is presented, based on a double-blind comparative test made on 22 pairs of patients. No significant difference was found between the effect of the two drugs. Both drugs were effective in improving the motive power and dullness of emotion. No significant difference was found between the type and frequency of the side effects of the two drugs, however, oxypertine tended to induce serious Parkinsonism and carpipramine induced serious stomach troubles such as vomiting and nausea. Half of the patients show a slowing-down of their EEG waves under administration of oxypertine. 23 references.

129273 Sano, Arata; Komatsu, Kaoru; Ando, Hajime; Hatagoshi, Hyozo. Jikei University School of Medicine, Tokyo, Japan Research on the defect state of schizophrenic patient under control of psychodrugs. *Clinical Psyciatry (Tokyo).* 12(11):35-39, 1970.

The defect state of the schizophrenic patient under control of psychodrugs was studied. Patients were observed twice within a two year period and compared to schizophrenics observed by Okuda in 1942 when no psychodrugs were used. Catatonic and paranoid types decreased under control of psychodrugs, however, hebephrenic and mixed types greatly increased. 20 references.

129451 Yamane, Hideo; Iizuka, Reiji. Department of Neuropsychiatry, Kyoto Prefectural University of Medicine, Kyoto, Japan A trial on the value of Sordinol in schizophrenia -- by subjective method and partly by using sequential analysis. *Clinical Psychiatry (Tokyo).* 12(3):211-218, 1970.

The effect of Sordinol (Clopenthixol, N746) on schizophrenia is reported. In a double-blind test, a sequential analysis was made of 37 male and 20 female chronic schizophrenic patients at Ryonan Hospital in Fukui Prefecture. The drug had very strong sedative, antihallucinatory, and antidelirium actions. The drug proved no more effective than a placebo in improving autistic tendency and spontaneity. 5 references.

129740 Yamauchi, Ikuro. Yamauchi Hospital, Japan Study on the effects of psychotropic drugs upon the photically driving theta response of electroencephalograms. *Clinical Psychiatry.* 12(1):25-32, 1970.

The effects of psychotropic drugs, such as diazepam and safrazine (beta-piperonylisoproplhydrazine) on the photically driven theta response of electroencephalograms and their clinical symptoms are reported. Diazepam was administered daily to 12 schizophrenic patients for one week. Seven patients out of 12 showed more photically driven theta response towards photical stimulus of 6.5HZ, and changes in clinical symptoms, such as improvement in communication, emotional expression, and decrease of autistic tendency. Safrazine was administered to 10 schizophrenic patients and the change in clinical symptoms is observed according to the change of photically driven theta response after three days of administration of the drug.

134906 Kishore, Baldew; Rajkumar; Kaur, Amarjeet. Punjab Mental Hospital, Amritsar, India Thiothixene in hospitalized chronic schizophrenic patients. *Indian Journal of Psychiatry (Madurai).* 12(4):225-237, 1970.

In a double-blind study of 60 hospitalized male chronic hebephrenic, catatonic schizophrenics, patients were treated in groups of 10 with prochlorperazine, trifluoperazine, thiothixene, thioproperazine, chlorpromazine and triflupromazine. Prochlorperazine was the most potent antipsychotic agent in these patients followed by thiothixene, triflupromazine and thioproperazine. Chlorpromazine and triflupromazine were found to be the least effective. Side-effects were frequent, being highest with thioproperazine followed by those with thiothixene, prochlorperazine and trifluoperazine respectively. They were minimal with chlorpromazine and triflupromazine. All the extrapyramidal side-effects except tremor could be controlled with ornaphenadrine hydrochloride (in 80-100%); tremor in only 57%. The side effects were not so severe as to cause a discontinuance of the drug administration. 13 references. (Author abstract modified)

138362 Bagadia, V. N.; Dave, K. P.; Shah, L. P. K.E.M. Hospital and Seth G. S. Medical College, Bombay-12, India A comparative study of physical treatments in schizophrenia. *Indian Journal of Psychiatry (Madurai).* 12(3):190-240, 1970.

A prospective study compared the efficacy of physical treatments in schizophrenia. Treatments included: electroconvulsive therapy; insulin subcoma therapy; chlorpromazine and trifluoperazine of the phenothiazine group; trifluperidol of the butyrophenone group; and flupenthixol of the thiaxanthine group. Eight hundred patients suffering from the disease were divided into six groups on the basis of prognosis. Improvement was considered significant when remission occurred in 50% or more of the symptoms. In overall improvement, total remission of symptoms and rapidity of improvement, electroconvulsive therapy proved superior to all other physical treatments; trifluoperazine and trifluperidol followed closely by chlorpromazine ranked second. Flupenthixol and insulin subcoma therapy were the least effective of the treatments tested. 14 references.

138597 McCarthy, Maureen. no address LSD as a diagnostic aid. *Unitas: a quarterly for the arts and sciences. (Manila, Philippines).* 43(2):3-35, 1970.

An investigation of the diagnostic values of lysergic acid diethylamide (LSD) as revealed by Rorschach protocols is reported. Subjects were eight female and two male psychiatric inpatients of the University of the East, Ramon Magsaysay Memorial Medical Hospital. It was found that LSD facilitates diagnosis of maladjustment and that the inner of psychological workings are most clearly amplified in the case of schizophrenics. Younger clinical subjects tended to give more overt reactions, but the age was not a deterrent since all post-LSD protocols confirmed the assigned personality classifications as accurate. The beneficial aspects of LSD for returnees were predicted only on a tentative basis. It is concluded that, under carefully supervised conditions, LSD can be harnessed for diagnostic purposes. 52 references.

138967 Jin, Sung Ki. National Mental Hospital, Korea Schizophrenia. *Official Journal of Research Institute of Medical Science of Korea.* 2(12):5-8, 1970.

Schizophrenia, hallucinations, delusions, negativism, and stupor are reviewed as occurring among the Korean teenage and young adult population. Until highschool graduation teenagers are usually overprotected, regimented, and consequently extremely immature. Thus, when suddenly exposed to adult society, they not only fail to understand it, but lack self-confidence and suffer from neuroses and other mental problems because of a perceived and often a real inability to cope with sexual, occupational, religious, and social problems. Emotional conflicts between the teenager and his parents further complicate the adjustment problems after leaving home. Chlorpromazine, trifluperazine, perphenazine, and thioridazine are mentioned as useful medicines.

139090 Kunugi, Hiroshi; Tamai, Yukiko; Mizuno, Shouji; Sakurai, Shunsuke; Saeki, Momoko; Saito, Chikako. Tokyo Tenshi Hospital, Japan The occupational therapy in a mental hospital for chronic schizophrenics. *Clinical Psychiatry (Tokyo).* 12(2):143-151, 1970.

Occupational therapy in a mental hospital for chronic schizophrenics is discussed. Four stages of occupational therapy are provided to patients including hospital wards; outside of the wards; and outside of the hospital. Therapy was given to 121 patients according to their working capacity, symptoms, and physical condition. During therapy, 37 patients regressed to a lower stage or dropped out. The major factor which resulted in failure was the interruption or decrease in dosage of psychotropic drugs. A table showing the relationship between the interruption or decrease in the dosage of drugs and failure is presented. The necessity of guiding patients to continue taking drugs is stressed. 13 references.

09 DRUG TRIALS IN AFFECTIVE DISORDERS

106763 Tupin, J.P. Department of Psychiatry, University of California, Davis, Calif. 95616 Certain circadian rhythms in manic-depressives and their response to lithium. *International Pharmacopsychiatry (Basel).* 5(2-4):227-232, 1970.

A subgroup of manic-depressives was noted to have a decreased range in the daily body temperature curve. The decrease in range did not differ in a statistically significant degree from normal controls and the other groups or manics. When given lithium the mean body temperature increased in both groups of manics but there was no change in the normal controls. Furthermore, in the manic group 2 there was a shift of the peak daily temperature from 6 pm to 12 noon. These data are discussed in the context of other observations of circadian rhythms in manic-depressives. 11 references. (Journal abstract)

106764 Platman, S.R. Department of Psychiatry, Downstate Medical Center, 450 Clarkson Avenue, Brooklyn, N.Y. 11203 Lithium carbonate: a drug of limited efficacy in the prevention of manic-depressive disease. *International Pharmacopsychiatry(Basel).* 5(2-4):132-136, 1970.

Forty nine manic-depressive patients were treated with lithium carbonate and 21 patients with imipramine in a single-blind study. In addition, a further 63 patients were treated with lithium carbonate in an open clinical study. Only 35 of the 112 patients treated with lithium carbonate remained well. Twenty seven patients required rehospitalization or outpatient shock treatment. Lithium carbonate proved superior to imipramine in the prevention of manic episodes. It was felt that lithium carbonate was a substance of weak clinical efficacy in the prevention of depressive attacks and of questionable efficacy in the prevention of some forms of recurrent manic episodes. 10 references. (Journal abstract)

106765 Klerman, G.L.; Paykel, E.S. Harvard Medical School, Massachusetts General Hospital, 2 Fruit Street, Boston, Ma. 02114 Long-term drug therapy in affective disorders: theoretical and methodological issues in current research on lithium. *International Pharmacopsychiatry (Basel).* 5(2-4):80-99, 1970.

The development of drugs for long-term treatment of the affective disorders depends upon the reconciliation of theoreticians and clinicians. Drug therapy relies upon the acknowledgement of the heterogeneity of depressions, and upon the revival of the disease concept of the affective disorders. Based upon these assumptions, lithium has been used in maintenance therapy. Further controlled studies are needed to conclusively demonstrate the efficacy of lithium in preventing recurrent depressive episodes. Although various research designs have a role in establishing the

overall efficacy of lithium, fully controlled double-blind studies are essential. Only further fully controlled studies can determine more definitely the states of lithium in the treatment of the affective disorders. 42 references. (Journal abstract)

106766 Schou, M.; Thomsen, K.; Baastrup, P.C. Psychopharmacology Research Unit, Aarhus University Institute of Psychiatry, 8240 Risskov, Denmark Studies on the course of recurrent endogenous affective disorders. ***International Pharmacopsychiatry (Basel).*** **5(2-4):100-106, 1970.**

A comparison of rates of relapse before lithium administration and after double-blind and open discontinuation was made. Results show 1) that the course of severe endogenous affective disorders is not easily influenced by the attitude of the doctor or the patient, and 2) that there is a high risk of further relapses in a group of patients who have had 2 or more episodes within a period of 2 years. 11 references. (Journal abstract modified)

106768 Coppen, A.; Bailey, J. West Park Hospital, Epsom, Surrey, England Sustained-release lithium carbonate. ***International Pharmacopsychiatry (Basel).*** **5(2-4):183-186, 1970.**

A form of sustained release lithium carbonate has been shown to give satisfactory plasma levels over several months administration. It enables lithium carbonate to be taken once a day, which is especially convenient and useful to patients on long-term prophylactic treatment of recurrent affective disorders. 10 references. (Journal abstract)

106771 Grof, P.; Cakuls, P.; Dostal, T. Department of Psychiatry, McMaster University, Hamilton, Ontario, Canada Lithium drop-outs: a follow-up study of patients who discontinued prophylactic treatment. ***International Pharmacopsychiatry (Basel).*** **5(2-4):162-169, 1970.**

Thirty three patients with recurrent affective disorder who stopped taking prophylactic lithium were followed up in 2 clinics and relapses recorded in open observation. After the discontinuation of lithium, the spontaneous course of the disease reappeared, with the relapse pattern resembling the one prior to the prophylaxis, or slightly deteriorated. 11 references. (Journal abstract)

106773 Freyhan, F.A.; O'Connell, R.A.; Mayo, J.A. Department of Psychiatry, St.Vincent's Hospital and Medical Center, New York, N.Y.

10011 Treatment of mood disorders with lithium carbonate. ***International Pharmacopsychiatry (Basel).*** **5(2-4):137-148, 1970.**

Study of the long-term effects of lithium on recurrent affective disorders is reported. Therapeutic, biological and adverse responses are discussed. Evidence points to therapeutic efficacy in patients with bipolar mood disorders. Therapeutic action appears to be reflected in a reduction of mood fluctuations resulting in lower frequency of hospitalizations. Some theoretical and clinical issues remain unsolved. Among these is the assumption of prophylaxis. Presently, evidence points to a compensatory mode of action which does not eradicate, but counteracts those symptom manifestations which accounted for higher frequency of hospitalization in the prelithium era. 5 references. (Journal abstract modified)

106774 Hofmann, G.; Hofer, R.; Joli, I.; Kremser, M.; Katschnig, H.; Scheiber, V. Allgemeines Krankenhaus der Stadt Wien, Psychiatrisch-Neurologische Universitatsklinik, Spitalgasse 23, A-1097 Vienna, Austria /Prophylactic action of lithium salts and thyroid hormones on symptoms of manic-depressive and affective psychoses: clinical and experimental results./ Die prophylaktische Wirkung von Lithiumsalzen und Schilddrusenhormon auf Manifestationen des manisch-depressiven Krankheitsgeschehens und der Legierungspsychosen: Klinische und experimentelle Ergebnisse. ***International Pharmacopsychiatry (Basel).*** **5(2-4):221-226, 1970.**

Lithium salts have been used since 1966 in the Psychiatric Department, University of Vienna Medical School. The therapeutic effect of lithium salts was evaluated on 119 patients. Statistically significant prolongation was observed of the cycle, defined as the time between the onset of one depressive phase until the onset of the next. The analysis of variances showed a significant correlation between duration of therapy and therapeutic effect. Schizoaffective disorders and chronic depressions were treated by a combination of lithium salts and thyroid hormones. With this combination, better therapeutic results could be achieved. 12 references. (Journal abstract modified)

106775 Mihovilovic, M. Department of Neurology and Psychiatry, School of Medicine, University of Zagreb, Zagreb, Yugoslavia Complications or coin-

cidences during lithium therapy: a review of several cases. *International Pharmacopsychiatry (Basel).* 5(2-4):218-220, 1970.

The question of whether somatic symptoms during lithium therapy are complications or coincidences is discussed. Some clinical observations on a sample of 35 female patients with typical recurrent manic-depressive psychoses, treated prophylactically with lithium carbonate over a 2-year period, are presented. Some common characteristics of the patients are noted (excluding a patient with thyroiditis); the symptoms are transient and periodical, the vascular system is affected, edemas are present, only the middle and lower parts of the limbs are attacked, mostly the areas near the joints. Three patients had their mania every time the symptoms appeared; 2 others had menstrual cycles. Edemas and capillary extravasations dominated in all cases. 4 references.

106777 Nahunek, K.; Svestka, J.; Rodova, A. Psychiatrische Universitatsklinik der medizinischen Fakultat der Universitat J.E.Purkyne, Brno, Czechoslovakia /Lithium's position among antidepressants in the treatment of acute endogenous and involutional depressions./ Zur Stellung des Lithiums in der Gruppe der Antidepressiva in der Behandlung von akuten endogenen und Involutionsdepressionen. *International Pharmacopsychiatry (Basel).* 5(2-4):249-257, 1970.

Lithium carbonate was used to treat 98 patients in the acute phase of endogenous depression and involutional melancholia; results were favorable in 54%. This approaches the rate of effectiveness of the tricyclical antidepressants. Qualitatively, the efficacy of lithium is well balanced, appearing in both retarded and anxious, agitated and atypical forms of depressions, as reflected in the value of the index of antidepressive effect. In this sense, the effect of lithium was close to that of trimeprimine, amitriptyline, proheptatriene, perathiepine and convulsive methods. The best results were obtained on an average in depression in which the intensity of initial symptoms was low. The patient's age, the number of phases experienced and the average blood serum lithium levels were not in any way correlated with the results of treatment. Side effects occurred in most cases, and in 4, signs of intoxication appeared, but the outcome was satisfactory. Lithium cannot be recommended as routine treatment for all cases of acute endogenous depression. It is intended to investigate the possible relationship between the result of treating the acute depressive phase with lithium and the response to subsequent prophylactic administration in the same patient. 3 references. (Journal abstract)

106781 Saran, B.M. Netherne Hospital, Coulsdon, Surrey, England The course of recurrent depressive illness in selected patients from a defined population. *International Pharmacopsychiatry (Basel).* 5(2-4):119-131, 1970.

All depressed patients from a population of 175000 who were hospitalized in 1965-1966 at least twice, were followed up for 3 years to find out whether their course could be predicted. Out of 53 patients who did not receive lithium, 40 could be followed to the end of the period. Each of these 40 patients was studied from January 1, 1965 to December 31, 1969. Fifteen patients diagnosed as reactive depression had a poorer prognosis than the rest. The remaining 25 spent only half the time in the hospital during the followup (89 days per year during control period, and 40 days per year during observation period), and the result is statistically significant. The number of admissions of these 25 patients was reduced to a quarter. This result is as good as that attributed to lithium by uncontrolled studies, whose evidence must therefore be retested. Whether the results of the present study are due to the selection criteria or the administration of psychotropic drugs or both could not be answered. 10 references. (Journal abstract)

109723 Rumyantseva, G.M.; Margolina, E.B. author address not given /Lithium as a therapeutic and preventive drug in affective disorders./ Litiy kak sredstvo terapii i profilaktiki affektivnykh rasstroystv. *Zhurnal nevropatologii i psikhiatrii imeni S.S.Korsakova (Moskva).* 70(7):1082-1090, 1970.

A survey is made of non-Soviet literature concerned with lithium as a therapeutic and preventive drug in affective disorders. The survey reveals that the use of lithium as a therapeutic substance is rather narrow due to its selective effect. Although the effectiveness of lithium in prevention of affective phases differs, it may be regarded positively as a rather effective substance for prevention of such disorders. The various methods of using lithium for treatment and prevention are outlined. The toxicity of lithium salts is negligible with proper use and consideration of all contraindications. 89 references.

111018 Shternberg, E.Ya. Institut psikhiatrii AMN SSSR, Moscow /Depressive states of old age and treatment of them./ Depressivnyye sostoyaniya pozdnego vozrasta i ikh lecheniye. *In: Shternberg, E., Problemy organizatsii psikhiatri.pomoshchi kliniki.* Moscow, Sovetskaya Rossiya, 1970. 130 p.(p.111-116), Part 1.

The different forms of mental disturbances are discussed with respect to recognition, nosographic diagnosis and treatment of depressive states in the aged. Comparison of the clinical and psychopathological aspects of depression in the aged and the characteristics of the psychotropic effect of various drugs permits the following conclusions: 1) since depressive syndromes in the aged are usually accompanied by internal anxiety or various degrees of an anxiety background of depressive effect, combined use of antidepressants and neuroleptic agents should gain preference over treatment with antidepressants alone, which often intensify anxiety in such cases; 2) a combination of tryptizol and aminazine or tryptizol and nozinan (tizercin) was effective in the greater markedness of the anxiety component; 3) the more pronounced are anxiety, anxiety - hypochondriacal, or anxiety - delirious symptoms in the pattern of depression, the greater should be the specific weight of sedative (neuroleptic) agents in combined treatment; and 4) in the presence of appropriate indicators, successful combined treatment of depressions in the aged also include use of tranquilizers or librium and valium.

112131 Fanali, A.; Nardini, M.; Sorgona, F. Clinica delle Malattie Nervose e Mentali, Universita di Siena, Siena, Italy /Effect of amantadine on the extrapyramidal syndromes induced by neuroleptics./ Azione della amantadina nelle sindromi extrapiramidali da neurolettici. *Sistemo Nervoso (Milano).* 22(5):273-285, 1970.

A double-blind study conducted in 12 psychotic patients revealed that oral administration of 1-2.5mg amantadine daily reduces significantly rigidity and akinesia induced by levopromazine, clopenthixol, haloperidol, and trifluperidol, given alone or in various combinations. During the 2 month study period, amantadine did not induce side-effects and did not affect the psychopathological condition of the patients, except for one instance of anxiety and insomnia which required the cessation of treatment. The group studied included cases of hallucinatory delirium, manic-depression and oligophrenia. 14 references.

114880 Cedrola, G.; Amati, A.; Del Vecchio, M.; Camardese, M.; Kemali, D. Clinica delle Malattie Nervose e Mentali, Universita di Napoli, Naples, Italy /Clinical results on the therapeutic action of lithium carbonate in dysthymic psychoses./ Rilievi clinici sull'azione terapeutica del litio carbonato nelle psicosi distimiche. *Ospedale Psichiatrico (Napoli).* 38(3):359-372, 1970.

Administration of lithium carbonate in daily doses of 900-1800mg, for 3-18 weeks, to 33 patients with manic depression resulted in complete clinical remission in 20, some improvement in 5 and no response in 8 of 11 patients with alternating manic depression, during a manic episode, 7 presented complete remission and 3 failed to respond. The respective failures in 8 similar patients treated during an episode of depression were 4 and 2. Of 5 manic patients, 4 had complete remission and 1 failed to respond. The respective figures for the 9 patients with obsession were 5 and 2. Four of the 5 manic patients had mediocre response to earlier treatment with chlorpromazine alone or associated with haloperidol. All 9 depressive cases had previous treatment with electroshock associated with amitryptyline and 6 of them obtained complete remission. Nine of the 11 manic-depressive patients, in manic episode, had complete remission to previous chlorpromazine and haloperidol, while the other 2 had partial remission to earlier reserpine associated with orphenadrine and thioridazine. Unspecified side-effects appeared in 2 patients but subsided upon cessation of treatment with lithium carbonate. 29 references.

118585 Hirai, Tomio; Yabe, Toru. Department of Neuro-psychiatry, Koishikawa Branch Hospital, School of Medicine, University of Tokyo, Tokyo, Japan The clinical effect of clomipramine (anafranil) as the anti-depressant. *Clinical Psychiatry (Tokyo).* 12(5):443, 1970.

The clinical effects of clomipramine (anafranil) as an antidepressant are reported. The drug was administered (75-150mg) intravenously to five patients for eight to 12 days. Blood pressure, pulse rate, body temperature, and EEG were recorded. The patients became free from anxiety and irritation, and in three out of five patients the depression was significantly lessened after three to six injections. The EEG showed an intermediary

rapid wave 20 to 25 minutes after the initial injection which was indicative of the remission of depression. No changes in the blood pressure, pulse rate, body temperature were observed; the drug proved particularly effective, for endogenous depression.

118730 Lapin, I.P. Leningradskiy nauchno-issledovatel'skiy psikhonevrologicheskiy institut imeni V.M.Bekhtereva, Leningrad, USSR /Pharmacological basis of antidepressant effects./ Farmacologicheskiye osnovy antidepressivnogo effekta. Leningrad, Ministerstvo Zdravookhraneniya RSFSR, 1970. 165 p.

The material for the symposium on antidepressants, held at the Bekhterev Institute between June 10 and 12, 1970, was divided into four main parts: the evaluation of antidepressants according to animal experiments; features of the biochemical pharmacology of antidepressants; the involvement of cerebral structures in the antidepressant effect; and clinical features of antidepressant pharmacology. Recent views on the pathogenesis of endogenous depression and selection criteria for the evaluation of new antidepressants are included. Catecholamine metabolism mechanisms involved in the pharmacological control of depression are discussed, as well as the action of antidepressants on the cerebral and somatic processes occurring in psychotic patients. The involvement of tryptophan in the antidepressant effect and monoaminoxidase inhibitor interactions with the central and peripheral serotonin reactive structures are analyzed. Combined action of antidepressant and neuroleptic drugs, the effect of phenamine and aminazine on behavioral inhibition and the effect of azaphene on the bioelectric activity of the brain constitute additional topics. The psychopathology of depression and the basic requirements of antidepressant pharmacology are reviewed.

126632 Amrumova, A.G.; Neduva, S.Sh. Klinikodispansernyy otdel moskovskogo nauchno-issledovatel'skogo instituta psikhiatrii MZ RSFSR, Moscow /The clinical aspects and dynamics of paranoiac psychopathy with malignant development./ Klinika i dinamika paranoicheskoy psikhopatii s sutyazhnym razvitiyem. *In: Shternberg, E., Prob.org.psikh.pom.klin.i epidem.psik.zabolev.* Moscow, Sovetskaya Rossiya, 1970. 130 p.(p.3-6), Part 1.

The evolution of paranoiac developments in psychopathy is surveyed from a historical standpoint. Specific cases are then cited for patients with paranoiac psychopathy, who are broken down into specific age groups. The nonuniformity of paranoiac development in the patients is discussed. Two variants of paranoiac psychopathy with various compensatory possibilities are distinguished. The first group includes patients whose illness was characterized by a slow increase of morbid experiences while retaining external features of normal behavior. Patients of the second group displayed extreme differential diagnostic complexity and clinical catamnestic investigations indicated the frequency of erroneous statements of schizophrenia in cases of the malignant variant of paranoiac psychopathy. Both groups of patients displayed varied reactions to neuroleptic agents used. A definite weakening of the morbid symptoms with improvement of compensation occurred in the first group, while the therapeutic effect of the drugs was negligible in the second group.

129452 Toru, Michio; Takamisawa, Misa; Tsuchiya, Kenji; Kobayashi, Teruyoshi; Kariya, Tetsuhiko; Shimazono, Yasuo. Tokyo Medical and Dental College, Tokyo, Japan A supplement to clinical evaluation of thiothixene with special reference to the treatment of affective psychoses. *Clinical Psychiatry (Tokyo).* 12(3):203-210, 1970.

The effect of thiothixene on affective psychoses such as schizophrenia and manic-depressive illness is reported. Thiothixene (5-40mg/day) was given to three subacute types and 13 chronic patients for two to five months. All of the subacute types and 46% of the chronic patients improved. Thiothixene (36mg/day) was administered to 21 chronic schizophrenic patients and two patients with remission for 6-16 months; 76% of the patients improved, and the relapse of the two patients was averted. No side-effect on liver or kidney function from long-term administration of the drug was observed. Of the 15 manic-depressives administered thiothixene, 80% showed significant improvement. 15 references.

129579 Noma, Takuji; Ohtsuki, Saburo; Watanabe, Masahiro; Yokoyama, Shigeo. Okayama University School of Medicine, Okayama, Japan The effects of lithium salts in the treatment of depression. *Clinical Psychiatry (Tokyo).* 12(1):65-66, 1970.

The effects of lithium salts in the treatment of mania and depression were examined. Lithium salts (300-350mg/day) were administered to 76 patients suffering from depression, and manic-depression. Lithium salts proved effective in the treatment of both mania and depression. It is suggested that the drug should be administered to patients suffering from chronic depression who have a ressistance to antidepressants. 7 references.

130414 Rapisarda, V.; Raffaele, R. Clinica delle malattie nervose e mentali dell'Universita di Catania, Catania, Italy /On the efficacy and the mechanism of action of lithium salts in manic-depressive psychoses./ Considerazioni sull'efficacia e sul meccanismo d'azione dei sali di litio nelle psicosi maniaco-depressive. *Ospedale Psichiatrico (Napoli).* 38(4):565-571, 1970.

The therapeutic use of lithium for treating manic-depressive psychoses is reviewed. The literature shows that lithium has been found effective in the treatment of manic states; it has not been proven clearly useful for treating acute depressions, but most researchers believe it capable of preventing recurrent depressions. The mechanism of action of lithium is discussed, with specific reference to the influence of lithium on the metabolism of sodium, potassium, calcium, and, to some extent, magnesium. Some hypotheses of theoretical and practical interest, suggested by the results of lithium therapy of dysthymic syndromes, are briefly discussed. In view of lithium's twofold effect on the neuronal membrane function and on the catecholamines, further research on the mechanism of such action should yield greater understanding of the relationship between the catecholamines and electrolytes in dysthymias. 17 references.

133147 Harrer, G. no address /Therapy with jatrosome./ Therapie mit Jatrosom. Stuttgart, Georg Thieme, 1970, 102 p. DM12.80.

A collection of contributions by well known specialists on therapy with jatrosome at the Salzburg symposium is presented. An appendix contains a report of the distribution and tolerance of this preparation and references to more than 102 cases treated with this drug. A comprehensive discussion includes a summary of the indications, contraindications, risk factors, as well as a hypothesis for the basis of a directed thymoleptic treatment in various types of depressive syndromes. This exposition on the treatment with jatrosome also includes a further aspect, its use in a combined therapy with tricyclic antidepressives and neuroleptics.

134902 Kumar, S.; Davis, R. B. Davis Institute of Neuropsychiatry, Boreya Road, Kanke, India Dexamethasone in depressive syndromes. *Indian Journal of Psychiatry (Madurai).* 12(4):260-263, 1970.

In a trial of 51 depressed patients, no advantage was noted in patients who were given dexamethasone as opposed to those who received a placebo. However, when dexamethasone was combined with imipramine, the results are comparatively better than combination of imipramine and a placebo. 1 reference.

134903 Teja, J. S.; Narang, R. L. Postgraduate Institute of Medical Education and Research, Chandigarh, India A double blind trial of three anti-depressants (GO 2998, GO 2330 and imipramine hydrochloride). *Indian Journal of Psychiatry (Madurai).* 12(4):253-259, 1970.

In a double-blind trial of three antidepressants, imipramine showed better results than GO-2330 and GO-2998 on the criteria of clinical improvement, percentage reduction of modified Hamilton's rating scale scores, and target symptoms of depression. GO-2330 was also found to be quite effective in all three criteria and resulted in the fewest side effects. GO-2998, the least effective of the three drugs, was responsible for the most side-effects. 4 references. (Journal abstract modified)

134940 Teja, J. S.; Agarwal, A. K.; Prabhu, G. G. Postgraduate Institute of Medical Education and Research, Chandigarh, India Protriptyline: a double blind cross over trial in depressives. *Indian Journal of Psychiatry (Madurai).* 12(4):244-252, 1970.

Protriptyline, an antidepressant of the tricyclic amino dibenzyl group, was studied in 65 hospitalized depressed patients. The drug was found to be superior to a placebo in treatment of all types of depression. It was particularly effective in psychotic depressives and involutional melancholia, with drug effect generally starting in the first week of treatment. Neurotic depressives showed poor response to the drug, complained of side-effects and tolerated only low dosages. Blood, urine and liver function studies revealed no abnormalities with drug treatment. Caution is suggested in using the drug with organic depres-

sives because it precipitates confusional states in predisposed patients. 3 references.

10 DRUG TRIALS IN NEUROSES

124308 Catalano, A. Istituto Psichiatrico 'S.Lazzaro', Reggio Emila, Italy /First orientations on the use of high doses of oxazepam, based on personal clinical therapeutic experience./ Primi orientamenti nell'impiego dell'oxazepam ad alte dosi, sulla base di una esperienza clinico-terapeutica personale. *Riv.Sper.di Fren.e Med.Legale delle Alienazione Ment. (Reggio Emilia).* 94(6):1628-1632, 1970.

Daily administration of oxazepam, for three weeks, in doses averaging 250mg and ranging from 100 to 475mg per day, to 30 patients with neuroses, personality disorders or psychoses induced optimal response in 18 and good response in eight. The response was highly significant against the somatic expressions of anxiety, hypochondria, cenesthesiopathy and antisocial behavior. No significant response was obtained in obsessive phobic manifestations and extrapyramidal syndromes. Slight transient side-effects consisting of sommolence, asthenia and orthostatic hypotension were noted in four cases. The compound was well tolerated even when given in doses higher than 400mg per day. 6 references.

129097 Nishizono, Masahisa; Murata, Toyohisa; Nagano, Mitsuo. Department of Psychiatry, Kyushu University School of Medicine, Japan A double blind comparison of S-804 (new benzodiazepine drug) with chlordiazepoxide and diazepam in the treatment of neurosis. *Clinical Psychiatry (Tokyo).* 12(10):883-887, 1970.

A report on the effect of S-804, a new benzodiazepine drug, on neurosis is presented, based on a double-blind comparison of the drug with chlordiazepoxide and diazepam made on 58 patients. S-804 was given to 27 patients with a daily oral dosage of 20 to 60mg, chlordiazepoxide was given to 22 patients with a daily oral dosage of 20 to 40mg, and diazepam to 9 patients with a daily oral dosage of 10 to 40mg for a period of two to 16 weeks. No significant difference exists in the type of neuroses, age group, period of dosage among the three groups of patients who received the three drugs. The results show that 63% of those who received S-804, 63.6% of those who received diazepam improved. No significant difference was found in the frequency and degree of seriousness of the drug's side-effects. It is concluded that S-804 is effective for anxiety, depression, autonomic nerve disorders, and is almost equivalent in effectiveness to chlordiazepoxide, but is less effective than diazepam. 3 references.

130714 Tandou, P. no address Preliminary experiences with 'Nobrium' in private psychiatric practice in Djakarta. *Far East Medical Journal (Hong Kong).* 6(8):222, 1970.

Preliminary experiences with Nobrium in private psychiatric practice in Djakarta, Indonesia, are reported. The study was done on 33 patients of whom the youngest was 17. Side effects were encountered in 13 patients, but 20 did not complain of any undesirable actions of the drug. The side effects consisted of drowsiness, dizziness and muscle weakness. They were very mild and disappeared in most cases after a few weeks of continued medication. The drug was effective in phobic and obsessive-compulsive conditions, which are difficult to abolish by drugs. It is concluded that Nobrium fills a vacant space in the spectrum of anxiolytic agents.

138526 Chaudhry, Mohammad Rashid; Ishaq, Mohd.; Suleman, M. Mayo Hospital, Lahore, Pakistan Double blind study with Sinequan (Doxepin) vs diazepam vs placebo in psychoneurosis. *Journal of the Pakistan Medical Association (Karachi).* 20(10):315-319, 1970.

In a double-blind trial, 40 patients with psychoneurosis of moderate to severe degree were treated with Doxepin, Diazepam or placebo for a period of four weeks. Doxepin hydrochloride was better tolerated and more effective than Diazepam or the placebo, and tranquilizing effects of Doxepin were more prominent. Symptoms cleared in nine patients with Doxepin, seven with Diazepam and two in the placebo group. Improvement on the Hamilton Anxiety Rating Scale also indicated that Doxepin was more effective. 13 references.

11 DRUG TRIALS IN MISCELLANEOUS DIAGNOSTIC GROUPS

101801 Benson, D.Frank. Boston University School of Medicine, Boston, Massachusetts /Dexedrine as an adjunct to aphasia therapy./ Presentation 10. *In: Benton, A., Behavioral change in cerebrovascular disease.* New York, Harper & Row, 1970. 257 p.(p.77).

The efficacy of Dexedrine as an adjunct during aphasia therapy is being investigated. The investigation is being done as 2 separate studies: one using patients who have been aphasic for over 6 months without significant language improvement, the other using patients who have been aphasic for 2 and 3 months. The first group acts as its own control, but both studies are double-blind. Half of the patients receive capsules with Dexedrine and half receive placebos. Extensive speech function and psychological testing is performed prior to treatment; the patients then enter into or continue aphasic therapy programs specific for their disorder. They remain in therapy 3 months and are fully retested at the end of the therapy period. They are retested again 1 month after the medication has been discontinued. Results will be published. Studies modeled on this investigation could be used for other studies of aphasia therapy.

105551 Korn, M. author address not given /An interesting tissulary therapeutic method in geriatrics: Bogomoletz' serum (Berna's cytotoxic serum)./ Une therapeutique tissulaire interessante en geriatrie: le serum de Bogomoletz (serum cytotoxique Berna). ***Feuillets Psychiatriques de Liege (Liege, Belgium).*** **3(1):81-85, 1970.**

The usefulness of Berna's cytotoxic serum, prepared according to Bogomoletz' method, in treating geriatric mental disturbances is briefly reported. Subcutaneous injection of this new drug in moderate doses has been found effective in various organic diseases, as well as in treating the psychological and psychiatric problems encountered during change of life and the beginning of senility. Based on preliminary case history observations such therapy is effective, and few side effects are noted when specific procedures are used and careful control over the duration of the drug's use is exercised. Various contraindications for its use, however, have been found and are listed.

105733 Horn, H.-J.; Luthe, R.; Schneider-Jonietz, B. Institut fur Gerichtliche Psychologie und Psychiatrie, Universitatskliniken, D-6650, Homburg/Saar, Germany /The medical and social indication of antiandrogen therapy./ Die medizinischen und soziale Indikation der Antiandrogen-Behandlung. ***International Pharmacopsychiatry (Basel).*** **5(1):23-26, 1970.**

The therapy with antiandrogen Cyproteroneacetate (Schering) represents a treatment of libido and sexual potency in men suffering under hypersexuality or deviation of sexual motive power; the method is reversible and always assessable to regulation. For 2.5years a total of 27 repeatedly prosecuted delinquents have been treated with this orally appliedbdrug. There was no counterindication related to the age of the men observed. A change of sexual motive powers or any result over and above the medication may not be expected. The best effects are to be expected from old men or younger married persons standing under afflicted power. Character defects or under standard intelligence oppose long-term, binding measures. (Author abstract)

109255 D'Amelio, Vincenzo. Ospedale neuropsichiatrico 'S.Maria Immacolata', Guidonia, Rome, Italy /A long acting neuroleptic in the treatment of chronic alcoholism in neurotic and psychotic patients./ Un neurolettico ad azione protratta nel trattamento delle tossicomanie alcooliche in soggetti nevrotici e psicotici. ***Igiene Mentale (Trapani, Italy).*** **14(4):681-687, 1970.**

Only 2 of 20 alcoholic females with neurotic manifestations (mainly depression and anxiety) who received sustained release Mellaril in daily doses of 400mg (for 2 months) presented alcohol withdrawal symptoms as compared to 4 of 10 such patients treated with disulfiram, tranquilizers and sedatives. One of 10 alcoholic females with psychotic symptomatology (schizophrenia, paranoia), treated with sustained release Mellaril daily doses of 600mg for 2 months, presented alcohol withdrawal symptoms as compared to 3 of 5 alcoholic psychotics treated with hypnotics and sedatives. In 90% of the patients treated with Mellaril, the response was manifested within the first 15 days of treatment, as compared to only 40% in the control group. In the Mellaril treated patients, the decreasing need for alcohol was accompanied by a decreasing neurotic symptomatology. 23 references.

109258 Tripi, Ettore. Ospedale Psichiatrico Provinciale, Trapani, Italy /Psychoclinical observations on the effect of the 'Logos' compound (association of pyrithioxine dihydrochloride, 1-tryptophan and calcium alpha-ketoglutarate)./ Osservazione psicocliniche sugli effetti del preparato denominato 'Logos' (associazione a base di piritiossina dicloridrato, 1-triptofano, alfa-chetoglutarato di calcio). ***Igiene Mentale (Trapani, Italy).*** **14(4):727-741, 1970.**

Ten mentally or physically retarded children between the age of 8 and 12 years, 10 patients aged 35 to 47 with reactive or endogenous depression and 10 patients aged 50 to 65 years with metabolic, vascular or senile mental deterioration were treated with Logos, in doses of 3 to 4 capsules daily, for 30 days. Matched control groups received placebos. Depressive patients also received thymoleptic drugs. Treatment resulted in satisfactory neurotonic and psychostimulant response in patients with mental retardation as well as in the group with mental deterioration. Slight euthymia was obtained in the patients with depression: in this group, the effect of antidepressants was more rapid. Treatment was well tolerated.

111028 Komova, Ye.A.; Lashinker, N.M. Kostromskaya oblastnaya psikhiatricheskaya bol'nitsa, Kostromo, USSR /Use of neuroleptics for vital indicators in patients with severe somatic states./ Primeneniye neyroleptikov po vital'nym pokazaniyam u bol'nykh s tyazhelym somaticheskim sostoyaniyem. *In: Shternberg, E., Problemy organizatsii psikhiatri.pomoshchi kliniki.* Moscow, Sovetskaya Rossiya, 1970. 130 p.(p.60-64), Part 1.

An attempt is made to generalize the experience of treating patients suffering from such mental states as catatonic arousal or stupor with pronounced negativism or prolonged refusal of food, amentive or delirious disorders accompanied by acute psychomotor arousal, depressive -paranoid syndrome with persecution complex and self-accusation, suicidal ideas and attempts at suicide and anxiety - depressive states with pronounced agitation. The somatic diseases of the patients included cardiovascular disease, disorders of the liver, lung disease, kidney disease, cancer of the stomach and arthrodial tuberculosis. The studies showed that, when using neuroleptic agents in treatment, it is unnecessary to terminate other treatment or to reduce the amount of treatment of the somatic disease, but the characteristics of the effect of each drug should be taken into account. Neuroleptic agents should be used in minimum doses in combination with other medicines and drugs to avoid aggravation of the physical condition of the patients. Specific examples are cited of increasing cardiovascular, hepatic or renal insufficiency which forced temporary termination of treatment with neuroleptic agents. No serious complications were observed in any of the 30 cases, but it is emphasized that use of neuroleptic agents to treat acute mental illnesses of patients with severe somatic diseases should be preceded by specific cautionary measures.

112130 Gentili, E. Clinica della Malattie Nervose e Mentali, Universita di Milano, Milan, Italy /Clinical evaluation of the use of G-32883 in trigeminal neuralgia./ Valutazioni cliniche sull'impiego del G-32883 nelle nevralgie trigeminali. *Sistema Nervoso (Milano).* 22(5):298-302, 1970.

Oral administration of carbamazepine to 40 patients with trigeminal neuralgia, including 2 with psychogenic neuralgia, induced complete response in 28, partial response in 5 and no response in 7. One of the patients with psychogenic neuralgia had complete remission of pain and the other failed to respond. Carbamazepine was given initially in daily doses of 100mg gradually increased up to 1000-1200mg for 1-2 weeks, and then maintenance treatment with 200-600mg. Treatment was well tolerated. 18 references.

126631 Volkova, R.P. Institut psikhiatrii AMN SSSR, Moscow /Clinical study of the drug Melleril./ Opyt klinicheskogo izucheniya preparata 'melleril.' *In: Shternberg, E., Prob.org.psikh.pom.klin.i epidem.psik.zabloev.* Moscow, Sovetskaya Rossiya, 1970. 130 p.(p.16-20), Part 1.

Pharmacological investigations showed that the drug Melleril (thioridazine), a piperidine derivative of phenothiazine, is very similar to chlorpromazine in the nature of its effects on the central nervous and vegetative systems. Clinical study of the drug and its retardative analogue was carried out on a group of 59 patients, most of whom were suffering from various types of schizophrenia. The patients ranged in age from 20 to 68 years and the average length of illness was 10 years. The drug was administered in tablets of 25 and 100mg and retardative Melleril was administered in tablets of 30 and 200mg. The patients were divided into 4 groups according to characteristics of the clinical pattern. The first group included those with torpid, periodic and paroxysmal schizophrenia, manic-depressive psychosis and involutional depression, the second group consisted of patients with maniacal and hypomaniacal arousal, the third group was characterized by psychopathic disorders and affective

instability and the fourth group displayed symptoms of paranoid schizophrenia. Treatment was relatively successful in the first 3 groups with varying degrees of effectiveness, while the drug had a more sedative effect in the fourth group. The tests show that the drug is effective for treatment of subdepressive, hypomaniacal and maniacal states, as well as in cases of continuing maniacal and depressive phases with psychopathic type disorders. The minimal toxicity and good tolerance indicate that use of Melleril and especially of its retardative analogue is more expedient and promising in ambulatory practice.

134937 Mahendru, R. K.; Gupta, S. C.; Agarwal, A. K.; Sethi, B. B. King George's Medical College, Lucknow, India Imipramine as an effective tool in the management of behavioral disorders in children. *Indian Journal of Psychiatry (Madurai).* 12(4):238-243, 1970.

Fifty children with enuresis and behavioral disorders were given imipramine (20 to 50mg) in divided doses for a period of three months. High percentage of recovery rate (76%) was noticed in enuresis, and encouraging results were obtained when the drug was administered in the management of obstinacy and temper tantrum. No significant improvement was noticed in some other behavioral disorders, especially when they were associated with mental retardation. No significant side effects were noted. 11 references.

138144 Haroon-Ahmed, S. Neuropsychiatric Unit, Jinnah Postgraduate Medical Centre, Karachi, Pakistan Neuropsychiatric manifestations in two cases of porphyria. *Journal of the Pakistan Medical Association (Karachi).* 20(1):13-17, 1970.

Two cases of porphyria are presented and neuropsychiatric manifestations, diagnostic methods, genetic aspects and management are reviewed. Both cases were treated with chlorpromazine, prednisolone and physiotherapy. The importance of nursing care and symptomatic treatment is stressed.

12 PSYCHOTOMIMETIC EVALUATION STUDIES

121085 Jarvik, M. Albert Einstein College of Medicine, Bronx, NY Drugs, hallucinations and memory. *In: Keup, W., Origin and mechanisms of hallucinations.* New York, Plenum Press, 1970. 479 p. (p. 277-301).

Diverse classes of drugs capable of producing hallucinations are reviewed. The anticholinergic drugs, the LSD family, and cannabis all cause hallucinations but produce different signs and symptoms and electroencephalographic changes and do not show cross tolerance. They seem to have in common the ability to impair discriminative learning and memory. It is proposed that hallucinations are a memory defect characterized by uninhibited retrieval and that one of the ways hallucinogenic drugs work is by impairing short term memory and inducing vicarious retrieval. 46 references.

121086 Fischer, R. Department of Psychiatry, Division of Behavioral Sciences, Ohio State University, Upham Hall, Columbus, OH Prediction and measurement of perceptual-behavioral change in drug-induced hallucinations. *In: Keup, W., Origin and mechanisms of hallucinations.* New York, Plenum Press, 1970. 479 p. (p. 303-332).

Prediction and measurement of perceptual behavioral change in drug induced hallucinations are discussed. After remodeling the old concept of hallucination as perceptions without an object to an operational definition of sensations without action, an attempt is made to quantify the high sensory to motor ratio, implicit in a hallucinatory experience by inducing the latter through the administration of psilocybin to college subjects, with handwriting area and pressure used as sensory and motor parameters. The results indicate that on the perception hallucination continuum of increasing levels of ergotropic arousal, hallucinations are characterized by increasing sensory to motor ratios, implying that higher and higher levels of arousal are accompanied by less and less freedom for the symbolic (perceptual - behavioral) interpretation of central nervous system activity. A biocybernetic model of conscious experience is described and noted to be validated elsewhere in neurophysiological terms. 67 references.

132911 Wyss, M.-A. no address /Intoxications by L.S.D.25: medicolegal problems./ Les intoxications par le L.S.D.25. Problemes medico-legaux. Paris, Masson et Cie, 1970. 159 p.

The historical background of the discovery of LSD-25 is presented, as well as a discussion of its physical and chemical properties, side-effects, and complications which can arise from use of the drug. Experimental data concerning its effects on humans and animals is reviewed, including

procedures for its identification and detection. Legal problems posed by adjudication of crimes committed under its influence are discussed. A description of a hallucinogenic trip is offered in a discussion of the drug's desocializing effects on users. The hallucinogens derived from LSD-25 are also examined.

13 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

100532 Shader, Richard I.; Giller, Donald R.; DiMascio, Alberto. Psychiatry Department, Massachusetts Mental Health Center, Harvard Medical School, Boston Hypothalamic-pituitary-adrenal axis. *In: Shader, R., Psychotropic drug side effects.* Baltimore, Williams and Wilkins, 1970. 290p.(p.16-24).

In a discussion of the effects of psychotropic drugs on endocrine and metabolic functions, action on the human hypothalamic - pituitary - adrenocortical axis is examined. Difficulties in assessing these effects are also stressed, including those stemming from differences in the release of adrenocorticotropin (ACTH) in man and in animals. The lack of exact methods of evaluating adrenocortical response is another problem. In view of the frequently reported dramatic effects of psychotropic drugs on the pituitary -adrenal axis of animals, it is of interest that adrenal insufficiency or hyperactivity often has not been attributed to their use in man, although there are numerous reports of at least minimal effects. Findings of several investigators have indicated possible inhibition of normal adrenocortical response in man following administration of phenothiazines and monoamine oxidase inhibitors, although much contradiction exists over the degree and mechanism of action. It appears most probable that the proposed mechanisms operate directly only in high dose animal research. In the human, it is more likely that psychotropic agents alter adrenocortical function primarily through their effects on emotion and behavior, rather than through any direct action on the hypothalamic - pituitary -adrenocortical axis. 59 references.

106767 Fieve, R.R. New York State Psychiatric Institute, 722 West 168th Street, New York, N.Y. 10032 Clinical controversies and theoretical mode of action of lithium carbonate. *International Pharmacopsychiatry (Basel).* 5(2-4):107-118, 1970.

Evidence to date indicates lithium's superiority over both placebo and probably phenothiazines for the treatment of mania. While it is premature to conclude that lithium is a proven prophylactic agent (since the evidence points both in positive and negative directions) this possibility could make lithium the first drug effective in the prevention of a major psychiatric disorder. From a number of investigations it is apparent that the physiological effects of lithium are numerous. Lithium alters monoamine metabolism and the EEG; it sustains nerve impulse conduction and affects the endocrine system; it produces significant changes in electrolyte balance and metabolism, and it may also alter intermediary metabolism. Because of the complex interrelationships among these various biochemical, electrical, and ionic events following lithium administration, it is difficult, if not impossible, to synthesize all the findings in these areas into any single unifying hypothesis with regard to lithium's mode of action. 50 references. (Author abstract modified)

106772 Helmchen, H.; Kanowski, S. Freie Universitat Berlin, Psychiatrische Klinik II, Nussbaumallee 36, D-1000 Berlin 19, Germany /Results of electroencephalographic studies relating to lithium efficacy./ Ergebnisse elektroenzephalographischer Untersuchungen zur Lithiumwirkung. *International Pharmacopsychiatry (Basel).* 5(2-4):149-161, 1970.

A survey of publications is given concerning the changes in EEG of patients under lithium treatment. First there is an increase of amplitudes of the background activity; later in therapy the background activity becomes more irregular with increased theta-frequencies(4-7/s). Also paroxysmal dysrhythmia or intermittent monorhythmic activities are frequently seen. Beside these changes there is an increased reagibility on hyperventilation. Some patients develop epileptic discharge under lithium treatment and even epileptic seizures may appear. EEGs during sleep show no gross changes. Lithium does influence cortical evoked responses in a special way and special lithium waves may be found in parts of the limbic system. All changes mentioned so far occur within the first 3 days of treatment. They can be seen under long lasting therapy and outlast the end of lithium treatment by 2 - 4 days. It is not clear if there is any correlation between EEG changes, serum concentration of lithium and the therapeutic effect. 15 references. (Journal abstract modified)

107549 Costa, E.; Garattini, S. author address not given International symposium on amphetamines and related compounds. New York, Raven Press, 1970. 936 p. $28.50.

Proceedings of an international symposium on amphetamines and related compounds are presented, with investigators using amphetamines as a means of investigating the autonomic and central nervous systems and studying the structure activity relationships of this compound and its derivatives in animals and man. New concepts are offered for the functions of amine containing systems in the brain, one of which is that dopamine may play a significant role in the behavioral changes these drugs produce. New insights are also given into the effect of these drugs on sleep, mood, and mental activity.

109786 Simich, S. author address not given /Physiological and biochemical mechanisms of the effect of lithium salts on the nervous system./ O fiziologicheskikh i biokhimicheskikh mekhanizmakh deystviya soley litiya na nervnuyu sistemu. *Zhurnal nevropatologii i psikhiatrii imeni S.S.Korsakova (Moskva).* 70(7):1091-1102, 1970.

A survey was made of literature concerned with the physiological and biochemical mechanisms of the effect of lithium salts on the nervous system. The various uses of lithium in treatment and prevention of affective disorders are outlined. It is concluded that, despite the extreme simplicity and elementary nature of its chemical structure, lithium has a multiple effect on the function of the nervous system, including a diffuse sedative effect on the central nervous system, the capacity to smooth out the periodicity of biological processes and the ability to render a definite and rather precise effect on exchange of cathecholamines in brain structures having adrenergic receptors. 86 references.

111961 Bogoch, Samuel; Dreyfus, Jack. author address not given The broad range of use of diphenylhydantoin: bibliography and review. New York, Dreyfus Medical Foundation, 1970. 169 p.

The literature on the basic mechanisms of action and the clinical uses of diphenylhydantoin are reviewed, and an extensive bibliography is presented. Considerable attention is paid to disorders of the nervous system, such as thought, mood, and behavior disorders, alcoholism and drug addiction, stuttering, and psychoses. Neurophysiologic mechanisms are discussed, such as peripheral nerve, spinal cord, neuromuscular junction and smooth muscle, and cerebral cortex and nuclei. Topics on biochemical mechanisms include acetylcholine in brain and heart, brain 5-hydroxytryptamine and tryptophane metabolism, and pituitary - adrenal function. There is a section on the chemistry of diphenylhydantoin and its metabolites, and another section covers the entry and binding of diphenylhydantoin in the brain. 750 references.

120899 Holden, J. M. C.; Itil, T. Department of Psychiatry, Missouri Institute of Psychiatry, University of Missouri School of Medicine, St. Louis, MO The influences of the standard prefrontal lobotomy operation on hallucinatory phenomena associated with psychotomimetic drugs. *In: Keup, W., Origin and mechanisms of hallucinations.* New York, Plenum Press, 1970. 479 p. (p. 37-51).

Some clinical and neurophysiological hypotheses concerning the mechanisms of hallucinations in groups of patients are described, using the psychotomimetic drugs LSD and Ditran as the investigatory tools. Clinical ratings are based on verbal evidence provided by the patient as well as overall clinical impressions. When rating hallucinations, the basic definition, 'perceptions without corresponding stimuli from without,' is applied. Results show some increase in overall schizophrenic psychopathology for the group, with corresponding EEG changes; more significantly, the neurological changes induced by the standard lobotomy operation facilitated the development of auditory, visual, and tactile hallucinations and disturbances of consciousness and higher mental function with LSD-25 in the chronic schizophrenic patient. The studies indicate that the orbital cortex is but part of a neurological complex of centers subserving emotional response and probably vigilance and memory to some degree, and also excitatory clinical and neurophysiological responses to LSD-25. The relationship between the orbital plate function and reticular formation activity is also considered, and mention is made of the contrasting effects of LSD and Ditran in the study. It is concluded that the study emphasizes the usefulness of combining clinical and objective forms of measurement such as the EEG in any structured research setting where the central effects of drugs are being investigated. 30 references.

121084 Herkert, E. E.; Keup, W. 681 Clarkson Avenue, Brooklyn, NY 11203 Disturbances in tryptamine serotonin metabolism associated with psychotic phenomena. *In: Keup, W., Origin and mechanisms of hallucinations.* New York, Plenum Press, 1970. 479 p. (p. 261-273).

Disturbances are reported in tryptamine - serotonin metabolism associated with psychotic phenomena. The data suggest, that high tryptamine levels may play a role in the development of a psychotic episode. This parallels previous findings that tryptamine excretion but not, to that degree, 5-HIAA excretion goes up during a psychotic episode. The nature of the connection between high tryptamine levels and behavioral changes is quite unclear. It is possible that N:N-dimethylation of tryptamine is facilitated when tryptamine levels are high. Tryptamine itself has a centrally excitatory effect similar to that of amphetamine, while serotonin is mainly a central depressant, and may have a protective function antagonizing the central excitatory effects of tryptamine. It is speculated that a similar biochemical constellation has existed in patients who became overtly psychotic, since their 5-HIAA output was reduced to about 1/3 of normal, while tryptamine output was not decreased. The conjunction of high tryptamine levels together with low serotonin levels might have contributed to the aggravation of their mental illness. 30 references.

129447 Nakazawa, Yoichi; Ushijima, Sadanobu. Hizen National Mental Sanatorium, Japan The effects of levomepromazine on the noctural sleep EEG in man. *The Kyushu Neuro-psychiatry (Fukuoka).* 16(1):68-76, 1970.

The effects of levomepromazine on the human nocturnal sleep EEG were studied. Levomepromazine was administered orally to five psychiatric patients; the daily dosage was gradually increased to maximum of 600-1500mg. Most spindle waves showed a prolongation of period, a drop in amplitude and a shortening of burst duration. REM sleep phase decreased with a small dosage of levomepromazine, however, its diminution was not exceeded beyond about 30% of REM sleep time of the premedication night. The inhibitory effects of levomepromazine are presumed to be located in the cortical and thalamocortical areas of the brain. 23 references. (Author abstract modified)

133861 Popova, N. K. Institut fiziologii, Sibirskoye otdeleniye Akademi nauk SSSR, Novosibirsk, USSR /Monoamine oxidase inhibitors and coronary insufficiency./ Ingibitory monoaminoksidazy i koronarnaya nedostatochnost'. Novosibirsk, USSR, Nauka, 1970. 196 p. $2.25.

The nature and mode of action of monoamine oxidase inhibitors on the ischemic heart are discussed. Data are presented on the biological role of monoamine oxidase and on the relationship of the physiological effects of its inhibitors with changes in tissue level of catecholamines and serotonin. Information on application of monoamine oxidase inhibitors in cases of angina pectoris and myocardial infarction, as well as experimental data on their effects on the development and course of ischemic damage of the myocardium are included. Previous research is extensively reviewed and original material dealing with the mechanism of the protective action of monoamine oxidase inhibitors in coronary insufficiency, and especially, ventricular fibrillation, is also presented. 713 references.

134932 Doongaji, Dinshaw R. K.E.M. Hospital, Bombay, India The Cinderella of psychopharmacology (a commentary on cannabis). *Bombay Hospital Journal (Bombay).* 12(2):15-18, 1970.

A discussion is presented on the use of marihuana. Topics include: 1) use in mythology and ancient history; 2) growth, cultivation and botanical features; 3) chemistry, pharmacology, and therapeutics; and 4) effects of short-term and prolonged use. The current controversy over effects is considered from standpoint of drawbacks of published studies. 16 references.

14 MECHANISM OF ACTION: BEHAVIORAL

103152 May, Joan Serber. University of Illinois at Urbana-Champaign The effects of an amphetamine on measures of intelligence and learning in mentally retarded adults. (Ph.D.dissertation). *Dissertation Abstracts International.* Ann Arbor, Mich., Univ.M-films, No.71-14860 HC$10.00 MF$4.00 79 p.

The effects of sudden stimulation of 10mg dextroamphetamine sulfate on the performance of 30 adult male mentally retarded patients on the Wechsler Adult Intelligence Scale and a paired associates learning task were assessed, using a double-blind, crossover design with 3 repeated measures. Data showed no effects of practice, order

of administration of drug, placebo and nothing, position of drug, or the drug factor itself on any of the dependent measures. A significant drug times session interaction was found for reaction time. (Journal abstract modified)

103301 Hallsten, Edwin Ansgar, Jr. University of Illinois at Urbana-Champaign State dependent recognition with methylphenidate and thioridazine in retarded children. (Ph.D.dissertation). *Dissertation Abstracts International.* Ann Arbor, Mich., Univ.M-films, No.71-14777 HC$10.00 MF$4.00 137 p.

An attempt to demonstrate whether or not state dependent learning would be found in conjunction with the administration of methylphenidate and thioridazine to mildly to moderately retarded children resident at a state school, ranging in age from 12 to 18, is reported. The task consisted of learning 24 pictures presented serially with a 1 second exposure and a variable interval. Recognition was probed immediately after training and after 24 hours. Hypotheses were developed concerning drug effects and state dependent learning. None of the hypotheses was supported. The only consistently significant effect observed was that for the retention interval. Evidence concerning the capability of the drugs tested to produce state dependent learning by these drugs under these conditions is clearly negative but should not be generalized to other tasks and dose levels. (Journal abstract modified)

103636 Comtois, Richard Joseph. University of Colorado Interpersonal understanding, interpersonal stress and current states: interrelationships and treatment assessment. (Ph.D. dissertation). *Dissertation Abstracts International.* Ann Arbor, Mich., Univ.M-films, No.71-21578 HC$10.00 MF$4.00 335 p.

An investigation of the effects of secobarbital (125mg) and methamphetamine (10mg) on interpersonal understanding, the handling of interpersonal stress, and a number of dimensions of self-report concerning the current state of subjects is reported. Subjects were 36 males, over 21 years of age with at least 2 years of college. They were divided into secobarbital, methamphetamine and control groups with each subject being assessed on the same procedures 2 times, once under drug and once under placebo for the drug groups, and once under placebo and once with no capsule for the controls. The only drug effects were predicted ones on the self-report questionnaire: a highly significant effect for secobarbital on the scale 'High' and a significant report for methamphetamine on the 'Happy and relaxed' scale. It appeared that subjects were able to avoid drug effects which would have been an interference in a very demanding situation. (Journal abstract modified)

105731 Tanimukai, H.; Inui, M.; Kaneko, Z. Department of Neuropsychiatry, Osaka University Medical School, Osaka, Japan Treatment and prophylaxis of manic states with a carbonic anhydrase inhibitor. *International Pharmacopsychiatry (Basel).* 5(1):35-43, 1970.

Considering the similarity of the change in electrolyte distribution after the administration of lithium preparations and of carbonic anhydrase inhibitors, an attempt was made at treatment and prophylaxis of manic states with benzanilamide, a carbonic anhydrase inhibitor. The following conclusions are tentatively drawn: (1) banzanilamide, at the oral dosage of 1,000-2,000mg/day, may have antimanic effects, though the potency seems to be somewhat weaker than that of lithium preparation; (2) benzanilamide may well prevent the manic episodes in a patient exhibiting frequent relapses; (3) benzanilamide may be superior to lithium preparation in prophylactic use for recurrent mania, since the former develops much less adverse reactions and can be used more safely than the latter. 15 references. (Author abstract modified)

105732 Hakola, P.; Venalainen, E.; Iivanainen, M. Psychiatrisches Hospital, Harjamaki, Finland /Experience with a combination of Amitriptyline and Thioridazine for the treatment of depressions./ Erfahrungen mit einer Kombination von Amitriptylin und Thioridazin bei der Behandlung von Depressionszustanden. *International Pharmacopsychiatry (Basel).* 5(1):16-22, 1970.

The combination of amitriptyline and thioridazine was tested in a total of 63 patients during depressive phases; no other psychotropic drugs were administered in addition within the period of treatment. The highest doses given daily to the patients amounted to 3 X 50 up to 75mg of amitriptyline and 3 X 50 up to 75mg of thioridazine. In most of the cases the depression showed its acute or first phase. The results were extremely good: nearly one half of patients (27/63) reached freedom of any symptom; the others improved significantly. It was found that

the tolerance of the combination was good. 7 references. (Author abstract modified)

105790 Suemitsu, Shigeru. Asahigawa Jido-in, Japan Problem behavior of children with severe mental and physical disorders -- experience of the use of Carbamazepine. ***Annual Report of Asahigawaso (Okayama).*** **3(1):68-71, 1970.**

A clinical report on the effect of Carbamazepine on problem behavior of 20 children with severe mental and physical disorders is presented. Results show that 9 of the children no longer exhibited problem behavior after the dosage, and most children showed a decrease in problem behavior. The liver trouble which appeared in one child cannot be considered as a side effect of this drug.

106762 Mayo, Julia A. Department of Psychiatry, Clinical Studies, St.Vincent's Hospital and Medical Center, New York, N.Y. 10011 Psychosocial profiles of patients on lithium treatment. ***International Pharmacopsychiatry (Basel).*** **5(2-4):190-202, 1970.**

A total of 44 patients who attended the lithium clinic for treatment of an affective disorder were investigated for psychosocial morbidity. Several studies were analyzed with respect to selected psychosocial variables. Findings were in accord with what has been reported on significant differences between bipolar and unipolar cases with respect to the following: bipolar cases have a lower age of onset, more hospitalizations, a positive family history of mania, a higher attempted suicide rate, higher social class, and a higher divorce rate. The study did not confirm reported findings with regard to a causal relationship between stressful events and hospitalization, loss of relative prior to age 15 or that a majority of first episodes in bipolar cases were of a depressive type. Other findings include a high incidence of alcoholism both in family history as well as in probands, among all subtypes; high rate of job and residential mobility notably among bipolar patients, and a consistently high self-image among bipolar patients in contrast to a low self-image amoung unipolar patients. Relatives report marked improvement in psychosocial stability of patients during lithium treatment. 16 references. (Journal abstract modified)

106776 Dostal, T.; Zvolsky, P. Psychiatric Research Institute, University Psychiatric Hospital, Prague 8, Czechoslovakia Antiaggressive effect of lithium salts in severe mentally retarded adolescents. ***International Pharmacopsychiatry (Basel).*** **5(2-4):203-207, 1970.**

Fourteen severe mentally retarded aggressive adolescents were administerd lithium for 8 months. The daily dosages of lithium were 6-48 mEq/patient, and the serum lithium level ranged between 0.30-0.95 mEq/l. Lithium seems to have a significant affect damping and antiaggressive effect in mentally defective male adolescents who had been previously resistant to phenothiazines. Excessive polydipsia connected with highly undisciplined fluid intake and polyuria connected with frequent bed wetting, however, represented a considerable limitation of the use of lithium in these states. 9 references. (Journal abstract)

109724 Yeryskev, O.F.; Mikhalenko, I.N. Otdel.farmakol.issled.i lecheniya psikhozov Leningradskogo NI psikhonevrologicheskogo instituta im.V.M.Bekhtereva, Leningrad, USSR /Use of melleril-retard in treatment of patients with depressive-paranoid and anxious-depressive syndromes. Opyt primeneniya preparata melleril-retard pri lechenii bol'nykh s depressivno-bredovym i trevozhno-depressivnym sindromami. ***Zhurnal nevropatologii i psikhiatrii imeni S.S.Korsakova (Moskva).*** **70(7):1055-1060, 1970.**

Melleril was used for prolonged treatment of 42 patients with different varieties of depressive conditions, such as schizophrenia and affective, involutional and vascular psychoses. A good therapeutic effect was obtained in 29 patients with predominantly affective disorders. The drug appeared to be especially effective in cases with expressed anxiety and phobic states. The antidepressive effect of Melleril is secondary and may be seen during the third or fourth week of treatment after its tranquilizing effect during the first days of treatment. The antipsychotic effect of the drug appears to be weaker and side effects are mildly expressed. It is concluded that the drug is highly effective in psychiatric practice. 21 references. (Journal abstract modified)

110896 Claridge, Gordon. author address not given Drugs and human behaviour. London, Penguin Press, 1970. 266 p.L2.40.

An account of some of the research on psychotropic drug effects and human behavior is provided. Topics of chief concern include placebos, memory, sleep, and individual dif-

ferences in drug response. Relatively little attention is paid to pharmacology, animal experiments, clinical studies, and therapeutics.

121083 Alpert, M.; Angrist, B.; Diamond, F.; Gershon, S. New York University School of Medicine, Department of Psychiatry, New York, NY Comparison of Ditran intoxication and acute alcohol psychoses. ***In: Keup, W., Origin and mechanisms of hallucinations.*** **New York, Plenum Press, 1970. 479 p. (p. 245-259).**

In a comparison of Ditran intoxication and acute alcohol psychoses, it is shown that Ditran can produce many of the phenomena seen in acute alcoholic psychoses. The finding of aspects of the hallucinosis and the tremulous delirium in an orderly dose response relation adds support to the impression that these conditions are related by a unitary pathological process in the alcohol withdrawal psychoses. The differences between Ditran intoxication and alcohol withdrawal may be related to differences between the duration of the experiment and the withdrawal. The model fits well enough to encourage a look for converging operations for further clarification. It is noted that subjects with an alcoholic history, especially with recent heavy drinking, are more sensitive to Ditran than other subjects. Although this sensitivity may reflect the action of nonspecific factors other vulnerable subjects do not show this sensitivity. There is an antagonist to Ditran which has a high degree of specificity. It is relatively inactive in relation to other psychotogens. 13 references.

121087 Bradley, R. J.; Johnston, V. S. Neuropsychology Laboratory, University of New Mexico, Albuquerque, NM 87106 Behavioral pharmacology of the hallucinogens. ***In: Keup, W., Origin and mechanisms of hallucinations.*** **New York, Plenum Press, 1970. 479 p. (p. 333-344).**

The features of the hallucinogenic molecule which are necessary for its unique effect are investigated in a study of the mode of action of the hallucinogens themselves. The avoidance paradigm, separated into two classes -- discrete avoidance and continuous avoidance -- is noted to be of considerable importance in investigating the behavioral pharmacology of amphetamine derivatives. Discriminated avoidance schedules employed in experiments with rats are reported, with emphasis on the action of mescaline. Further research is described for the derivatives of tryptamine. 21 references.

126180 Lehmann, Heinz E.; Ban, Thomas A. no address Pharmacotherapy of tension and anxiety. Springfield, Illinois, Thomas, 1970. 129 p.

The history, classification, behavioral effects, and possible mechanisms of actions for the various categories of drugs used to treat anxiety are presented. It is suggested that the rational approach to anxiety is through psychotherapy and that pharmacotherapy of anxiety should be considered a secondary approach.

128568 Schuffel, W.; Schaumburg, Cornelia. Abteilung fur Psychosomatik des Zentrums Innere Medizin und Kinderheilkunde der Universitat Ulm, D-79 Ulm, Germany Tranquilizers in the treatment of the cardiac neurotic patient and the subsequent alteration of complaints. ***Psychotherapy and Psychosomatics (Basel).*** **18(1-6):307-312, 1970.**

A study of tranquilizers in the treatment of the cardiac neurotic patient and the subsequent alteration of complaints is reported. Fifty one cardiac neurotic patients were administered a new benzodiazepin derivate (Dikalium-Chlorazepat) over a three week period under the conditions of a double-blind trial. The scores of the heart items on the recently developed Zenz list of somatic complaints were significantly reduced in the drug group whereas the scores of the other items on the same list remained stable. However there was no significant difference between the desire for continuation and terminating the treatment. The following conclusions are applicable: cardiac neurotic patients react according to mechanisms which are recognized in psychophysiology as certain kinds of stereotypy; they seem to experience less stressful events when under the influence of Dikalium-Chlorazepat; experiencing less somatic complaints and possibly less stress when under drug does not necessarily mean that the therapeutic situation is regarded as positive; a critical double-blind study has to be able to account for the subjective meaning of the therapeutic criteria being applied. 8 references. (Author abstract)

133916 Baust, W. no address /Fatigue, sleep and dreams./ Ermudung, Schlaf und Traum. Stuttgart, Wissenschaftliche Verlagsgesellschaft, 1970. 314 p. DM 68.00.

The state of sleep research is reviewed; older theories aspiring to total explanation of neurophysiological processes are rejected in favor of a piecemeal approach. Neuroanatomical problems encountered in connection with regulatory principles are outlined. Circadian rhythms are examined

as possible grounds for the periodicity of sleep. Disturbances of sleep are described; possibilities of pharmacological sleep induction are explored.

133935 Simko, A. no address /Psychopathology of tranquilizer abuse./ Zur Psychopathologie des Tranquilizer-Abusus. *Alcoholism (Zagreb).* 6(1):7-10, 1970.

Habituation, withdrawal and abstention problems and effect on personality resulting from prolonged treatment with tranquilizers are discussed, in particular such character modifications as inauthentic adaptation, fixed posturing and a lowering of the frustration threshold. In contrast to the user of opiates, who is interested primarily in an ecstatic separation from reality, the tranquilizer addict merely wants to be rid of discomfort. Asthenics are particularly prone to abuse depressants. Mental tension states signal a situation with which the patient cannot cope; the neutralization of such physiological tensions with the aid of drugs may have deleterious consequences for the individual and society. A sample of 356 patients treated for three months because of neurotic functional or depressive anxiety complaints developed an addiction rate of 11%. 9 references. (Author abstract modified)

135186 Lynch, William John. University of Tennessee The performance of LSD users on certain neuropsychological tests. (Ph.D. dissertation). *Dissertation Abstracts International.* Ann Arbor, Mich., Univ. M-films, No. 71-7651 HC$10.00 MF$4.00 74p.

A group of 16 White, young adults who claimed to have taken LSD at least once were compared on a series of psychological tests with a control group of the same size. The groups had similar level of education, age, and socioeconomic background. The tests employed included the Wechsler Adult Intelligence Scale (WAIS), Halstead-Reitan Neuropsychological Battery and Minnesota Multiphasic Personality Inventory (MMPI). Significant intergroup differences were found on the following tests: Object Assembly Subtest of the WAIS and on the F (false) and MA (hypomania) scales on the MMPI. The results are interpreted as failing to support the hypothesis that LSD use causes demonstrable brain damage. Differences between the LSD user and the nonuser's personality are discussed. The difficulties and shortcomings of the post facto design employed are considered and possible improvements are suggested. (Journal abstract modified)

15 TOXICOLOGY AND SIDE EFFECTS

100514 Ebert, Michael H.; Shader, Richard I. Psychiatry Department, Massachusetts Mental Health Center, Harvard Medical School, Boston Cardiovascular effects. *In: Shader, R., Psychotropic drug side effects.* Baltimore, Williams & Wilkins, 1970. 290 p.(p.149-163).

The cardiovascular side effects of the major psychotropic drugs presently in use are reviewed. In addition, the use of such drugs in individuals with cardiovascular disease is considered as they are being increasingly administered in the management of such patients. Major focus is on the phenothiazines and antidepressants, since these agents have significant and common cardiovascular actions. These include effects on blood pressure and pulse, electrocardiographic changes, and arrhythmias and sudden death. In clinical practice today, the choice of which antianxiety agent to use is largely made on the basis of personal preference. Certain properties of these drugs should be kept in mind when treating patients with coronary artery disease. Phenobarbital has the disadvantage of being a general central nervous system depressant and of interfering with the anticoagulant activity of coumarin drugs by enzyme induction in the liver in susceptible patients. Recently, it has seemed that the benzodiazepine group of minor tranquilizers might be more appropriate for these patients. Further investigation in this area is sorely needed. 76 references.

100515 Shader, Richard I.; Belfer, Myron L.; DiMascio, Alberto. Psychiatry Department, Massachusetts Mental Health Center, Harvard Medical School, Boston Glucose metabolism. *In: Shader, R., Psychotropic drug side effects.* Baltimore, Williams & Wilkins, 1970. 290 p.(p.46-62).

In a discussion of the effects of psychotropic drugs on endocrine and metabolic function, the action on glucose, or carbohydrate, metabolism is examined. Research on the nature of carbohydrate metabolism in the mentally ill and the response following administration of a number of psychotropic drugs is reviewed and case history material presented. From these analyses, it appears that phenothiazines have a hyperglycemic effect in some patients. Phenothiazines cannot, at this time, be considered to be causes of diabetes mellitus, but they may alter the threshold and thereby expose latent or prediabetic patients. It remains to be explained why neuropsychiatric pa-

tients, in general, appear to have a higher incidence of blood glucose elevations than the general population. There may be meaningful drug diagnosis interactions. Benzodiazepines also may increase glucose but probably even less frequently than the phenothiazines, while meprobamate does not appear to cause such increases. Tricyclic antidepressants may lower blood glucose, particularly in diabetic patients. This hypoglycemic effect is clearer with MAOI drugs and may represent a potential hazard if such drugs are given to patients who are concomitantly receiving insulin or sulfonylurea derivatives. 88 references. (Author abstract modified)

100516 Shader, Richard I.; DiMascio, Alberto. Psychiatry Department, Massachusetts Mental Health Center, Harvard Medical School, Boston Psychotropic drug side effects: clinical and theoretical perspectives. Baltimore, Williams & Wilkins, 1970. 290 p.

Current research findings and clinical practices related to the administration of psychotropic drugs in treating psychiatric disturbances are discussed with respect to the toxicity and side effects of such compounds. Topics include the effects of psychotropic agents on the endocrine, metabolic, sexual, dermatological, neurological, and opthalmological functions of the body, as well as specific discussions of their behavioral action. These behavioral effects are examined in detail for the psychomotor, perceptual - cognitive, and emotional (mood) aspects of human performance. Physiological considerations include cardiovascular, hematological, hepatic, and gastrointestinal effects of psychotropic drug treatment. Finally, special mention is made of the use of such compounds during pregnancy and in the treatment of children and the elderly.

100517 DiMascio, Alberto; Soltys, John J.; Shader, Richard I. Psychiatry Dept., Tufts Medical School, Mass. Psychotropic drug side effects in children. *In: Shader, R., Psychotropic drug side effects.* Baltimore, Williams & Wilkins, 1970. 290 p.(p.235-260).

A review is presented of the adverse and toxic actions of psychotropic drugs in children, emphasizing the relative lack of systematic data in this area. The categories of psychotropic compounds most often used in child therapy are identified, and comment is made on the various side effects they produce or on the organ systems they affect. These drugs are: 1) antipsychotic agents, including chlorpromazine, thioridazine, trifluoperazine, perphenazine, fluphenazine, thioxanthenes, and butyrophenones; 2) antidepressant agents, including amitriptyline, imipramine, and monoamine oxidase inhibitors; 3) antianxiety agents, including chlordiazepoxide, diazepam, and meprobamate; and 4) stimulants, including amphetamines, and methylphenidate. 109 references.

100518 Greenblatt, David J.; Shader, Richard I. Harvard Medical School, Boston Acute poisoning with psychotropic drugs. *In: Shader, R., Psychotropic drug side effects.* Baltimore, Williams & Wilkins, 1970. 290 p.(p.214-234).

The incidence of acute poisoning with psychotropic drugs is discussed and compared with the toxicity of barbiturates. It is found that psychotropic drugs, although prescribed as often as the barbiturates, account for only a small percentage of fatal intoxications. The major tranquilizers, such as phenothiazines, have a wide margin of safety and cases of overdose nearly always have a nonlethal outcome. Of the minor tranquilizers, or antianxiety agents, the benzodiazepine derivatives are extremely nontoxic, while meprobamate carries a limited hazard as compared with barbiturates. Poisoning can also result from misuse of the antidepressants and is a problem to physicians, since they are usually prescribed to depressed and suicidal patients. The methodology for detoxification in this situation is described. Concerning the toxicity of the psychotropic drugs, it is concluded that they are relatively safe as compared with the barbiturates and glutethimides. Use of the latter compounds with depressed or anxiety ridden patients should be avoided. For tranquilizing action in anxious or neurotic patients, benzodiazepines are recommended over meprobamate and other psychotropic drugs both in terms of effectiveness and toxicity. 58 references.

100519 Shader, Richard I. Psychiatry Department, Massachusetts Mental Health Center, Harvard Medical School, Boston Pregnancy and psychotropic drugs. *In: Shader, R., Psychotropic drug side effects.* Baltimore, Williams & Wilkins, 1970. 290 p.(p.206-213).

The use of psychotropic drugs during pregnancy is discussed, emphasizing that although no harmful side effects may be detected in the

mother during this period, there is the possibility of harm to the unborn infant. Based on a review of relevant literature, it is concluded that neonatal effects, which at present seem entirely reversible, may be noted when psychotropic drugs are used during the last trimester or during labor. From these observations and from laboratory animal work it appears that some, if not all, such drugs are definitely able to cross the placenta. Limited available data indicate that the effects of chlorpromazine (the only one of the drugs sufficiently tested) on nursing infants are insignificant. Finally, the specific possibility that phenothiazines can induce neonatal jaundice and hyperbilirubinemia has not been settled. 31 references.

100520 Shader, Richard I.; Harmatz, Jerold S. Psychiatry Department, Massachusetts Mental Health Center, Harvard Medical School, Boston Gastrointestinal effects. *In: Shader, R., Psychotropic drug side effects.* Baltimore, Williams & Wilkins, 1970. 290 p.(p.198-205).

The influence of psychotropic drugs on various aspects of gastrointestinal (GI) tract functioning is discussed. Typical side effects of these drugs include nausea and vomiting, dysphagia, dry mouth, constipation, paralytic ileus, diarrhea, and decreased gastric secretion. These symptoms differ in form and degree with individuals, dosage, and choice of drug prescribed. In contrast, many psychotropic drugs, either alone or in combination with other anticholinergic agents, have been employed with a degree of success in treating GI disturbances. 32 references.

100521 Ebert, Michael H.; Shader, Richard I. Psychiatry Department, Massachusetts Mental Health Center, Harvard Medical School, Boston Hepatic effects. *In: Shader, R., Psychotropic drug side effects.* Baltimore, Williams & Wilkins, 1970. 290 p.(p.175-197).

The various physiological interactions between psychotropic agents and the liver are examined in a discussion of the hepatic effects of these drugs. Most literature on the hepatotoxicity of phenothiazines concerns chlorpromazine. A braod spectrum of severity in hepatic illness exists, with the typical characteristic in chlorpromazine induced liver disease being the appearance of jaundice. Laboratory findings in chlorpormazine hepatitis ressemble those found in other types of obstructive jaundice, and a consistent pattern of histopathological findings is apparent. Incidence of the disease due to chlorpromazine administration is difficult to estimate, but records of treatment of acute psychiatric illness over a relatively short hospitalization at one institution indicate that it is relatively rare. Management of the condition at the institution is described with case history material. Other drugs with potential hepatotoxic effects include tricyclic antidepressants, minor tranquilizers, butyrophenones and thioxanthenes, and monoamine oxidase inhibitors. Additionally, enzyme induction is another form of liver impairment possibly caused by psychotropic drugs. 102 references.

100522 Ebert, Michael H.; Shader, Richard I. Psychiatry Department, Massachusetts Mental Health Center, Harvard Medical School, Boston Hematological effects. *In: Shader, R., Psychotropic drug side effects.* Baltimore, Williams & Wilkins, 1970. 290 p.(p.164-174).

Drug induced blood dyscrasias are examined in a discussion of the hematological effects of psychotropic drug therapy. These dyscrasias include: agranulocytosis, aplastic anemia, and thrombocytopenic purpura. Although these conditions are rare side effects, the most common form is agranulocytosis, and all are generally brought about by use of phenothiazine derivatives and imipramine and meprobamate. Symptoms and diagnostic procedures in suspected cases are described, as well as the primary management principles. Finally, the typical features of agranulocytosis induced by phenothiazines and tricyclic antidepressants are illustrated with case history material. 50 references.

100523 DiMascio, Alberto; Shader, Richard I.; Giller, Donald R. Psychiatry Dept., Tufts Medical School, Mass. Behavioral toxicity. Part 3: perceptual-cognitive functions and Part 4: emotional (mood) states. *In: Shader, R., Psychotropic drug side effects.* Baltimore, Williams & Wilkins, 1970. 290 p.(p.132-141).

The behavioral toxic effects of psychotropic drugs as they pertain to perceptual - cognitive functions and to emotional (mood) states are summarized. It is seen that drug induced alterations in perceptual phenomena include impairment of such diverse processes as size estimation, auditory discrimination, detection of apparent motion, concentration and focus of attention, and rate of stimuli influx per unit time. Since these are

laboratory based observations, however, they have little predictive value for more complex non-laboratory situations, and such complications have not been widely reported in clinical situations. Considerable data have also been accumulated on the effects of psychotropic drugs on such cognitive processes as memory, reasoning ability, mental speed and learning. Insofar as emotional states are concerned, paradoxical drug effects have been cited which involve alterations in mood in a direction opposite to the clinically desirable one for which the drug is prescribed. These include increased anxiety and acts of rage and violence, chiefly stemming from the benzodiazepines, phenothiazines, monoamine oxidase inhibitors, and imipramine. 90 references.

100524 DiMascio, Alberto; Shader, Richard I. Psychiatry Dept., Tufts Medical School, Mass. Behavioral toxicity. Part 1: definition and Part 2: psychomotor functions. *In: Shader, R., Psychotropic drug side effects.* Baltimore, Williams & Wilkins, 1970. 290 p.(p.124-131).

The nature of behavioral toxicity in mentally or emotionally disturbed persons brought on by the administration of psychotropic drugs is defined, and specific effects on psychomotor functions are described. Behavioral toxicity is a phrase used to denote those pharmacological actions of a drug that, when administered within the dosage range in which it has been found to possess clinical utility, produce alterations in perceptual and cognitive functions, psychomotor performance, motivation, mood, interpersonal relationships, or intrapsychic processes of an individual to the degree that they interfere with his capacity to function within his setting or constitute a hazard to his physical well-being. Antipsychotic, antidepressant, and antianxiety drugs can all exhibit behavorial toxicity. A brief review of the literature is provided to show the psychomotor aspects in which these drugs interfere with muscular activities as a response to environmental stimuli. These include reaction time, dexterity, speed of activity, and steadiness. Considerable material exists showing drug induced decrements in laboratory tests of these skills, particularly in the areas of automobile and industrial accidents. 34 references.

100525 Belfer, Myron L.; Shader, Richard I. Harvard Medical School, Boston Autonomic effects. *In: Shader, R., Psychotropic drug side effects.* Baltimore, Williams & Wilkins, 1970. 290 p.(p.116-123).

Autonomic nervous system effects caused by administration of psychotropic drugs are discussed. It is stressed that both adrenergic and cholinergic systems may be affected and that although a particular drug may have one predominant effect, there are usually additional ones. Autonomic side effects are mild and tend to diminish after several weeks of treatment, but the physician should be aware that psychotropic drugs may potentiate the anticholinergic effects of other drugs. Difficulty also frequently arises in differentiating drug induced side effects from the symptoms of the illness for which they have been prescribed. The primary conditions found to be related to psychotropic drugs include: (1) blurred vision, (2) glaucoma, (3) urinary retention, and (4) perspiration. 30 references.

100526 Shader, Richard I.; Appleton, William S.; DiMascio, Alberto. Psychiatry Department, Massachusetts Mental Health Center, Harvard Medical School, Boston Ophthalmological (pigmentary) changes. *In: Shader, R., Psychotropic drug side effects.* Baltimore, Williams & Wilkins, 1970. 290 p.(p.107-115).

Ophthalmological changes caused by administration of psychotropic drugs are described and illustrated with case material. These complications include tardive dyskinesias and pigmentary changes in the eye, and are chiefly the result of long-term chlorpromazine treatment. A number of difficulties in differentiating drug induced changes from other causes of corneal and lens opacities are stressed and methodological and therapeutic factors are also discussed. Chlorpromazine induced opacities result from an accumulation of deposits, the nature of which has not yet been defined. Investigators agree that such corneal and lens deposits do not interfere with visual acuity until they reach a very advanced stage. The occurrence of these complications is definitely a dose related phenomenon. Other ophthalmological effects of psychotropic drugs include epithelial keratopathy, a condition characterized by white, gray, and brown opacities of different formation, and pigmentary retinopathy, a pigmentary change in the retina resulting from chlopromazine or thioridazine treatment. Since this condition can cause drastic reduction in visual acuity or blindness and can only be detected by ophthalmoscope, patients should receive intensive examination before drug therapy begins if long-term or high dose regimens are anticipated. 32 references.

100527 Greenblatt, David J.; Shader, Richard I.; DiMascio, Alberto. Harvard Medical School, Boston Extrapyramidal effects. *In: Shader, R., Psychotropic drug side effects.* Baltimore, Williams & Wilkins, 1970. 290 p.(p.92-106).

Side effects of the administration of psychotropic drugs on the extrapyramidal system (EPS) are discussed and illustrated with case history material. Historically the phenothiazine tranquilizers, or neuroleptics, were the agents most often associated with EPS disorders, but recent investigations have revealed similar reactions to butyrophenones and thioxanthenes. The incidence and severity of reaction depends on dosage, length of treatment, and individual susceptibility. Most drug induced extrapyramidal disorders are entirely reversible and disappear soon after discontinuation or lowering of drug dosage. These reversible disorders fall into 3 broad categories: (1) dystonic reactions, (2) akathisia or motor restlessness, and (3) parkinsonian reactions. Treatment usually involves simultaneous therapy with any of a number of synthetic antispasmodic parasympatholytic agents. However, the pressing need for more effective methods of treating both naturally occurring and drug induced extrapyramidal disorders is stressed, and some recent findings in the biochemical research field are reported. These include the use of dopamine, the biosynthetic precursor of norepinephrine and its precursor, DOPA. 54 references.

100528 Shader, Richard I.; Salzman, Carl; DiMascio, Alberto. Psychiatry Department, Massachusetts Mental Health Center, Harvard Medical School, Boston Collagen disease-like reactions. *In: Shader, R., Psychotropic drug side effects.* Baltimore, Williams & Wilkins, 1970. 290 p.(p.86-91).

The occurrence of collagen disease reactions, or lupus-like syndromes, in patients under treatment with psychotropic drugs is discussed. Analysis of relevant research and clinical experience indicates that the most frequent causative agent in this condition appears to be hydralazine. Additional drugs known to produce such a syndrome include: procainamide, iodides, heavy metals, trimethadione, antibiotics, sulfonamides, thiourea derivatives, diphenylhydantoin, and isoniazid. Reactions range from simple migratory polyarthritis and/or polyarthralgia and skin rash to acute systemic lupus erythematosus, characterized by a number of severe manifestations. It is stressed, however, that drug induced collagen reactions may represent the unmasking of an unsuspected or latent disease in the same way that barbiturates may precipitate porphyria. For this reason, the role of these drugs as etiological factors requires intensified research, as noted by the findings in several case histories. Of particular importance are host factors, or genetic predispositions, and environmental factors, including the use of high risk drugs. Drug induced collagen disease-like syndromes remit when the offending drug is withdrawn. 12 references.

100529 Appleton, William S.; Shader, Richard I.; DiMascio, Alberto. Psychiatry Department, Massachusetts Mental Health Center, Harvard Medical School, Boston Dermatological effects. *In: Shader, R., Psychotropic drug side effects.* Baltimore, Williams & Wilkins, 1970. 290 p.(p.77-85).

The dermatological effects of psychotropic drug administration are examined and case material is presented, emphasizing that such common side effects pose interesting problems in diagnosis, prevention, and management. The wide variety of skin disorders produced by psychoactive agents can be divided into 2 categories: (1) simple allergic skin reactions and (2) light related reactions. The former condition occurs in 3 forms, the most common of which is a maculopapular rash on several parts of the body. Light related reactions (phototoxicity) are thought to result from the ability of certain substances to absorb light energy of wavelengths shorter than 4000 angstroms. Photosensitive reactions to phenothiazines, particularly chlorpromazine, are the most common. A rare side effect, usually occurring after years of phenothiazine treatment, is pigmentation changes. Physicians should avoid long-term, high dose phenothiazine regimens whenever possible to prevent this condition. 26 references.

100530 Shader, Richard I. Psychiatry Department, Massachusetts Mental Health Center, Harvard Medical School, Boston Male sexual function. *In: Shader, R., Psychotropic drug side effects.* Baltimore, Williams & Wilkins, 1970. 290 p.(p.63-71).

The effects of psychotropic drugs on the male sexual function are discussed, and relevant animal research is reviewed. Studies showed that reserpine produces regressive and atrophic changes in testes (particularly the interstitial cells) of rats and birds. Many changes in animals have been reported following phenothiazine administration ranging from reduction in the percentage of motile

sperm to testicular changes such as degeneration of the seminiferous tubules and impaired spermatogenesis. There have been very few such studies in humans, and their results are extremely controversial. These contradictions are illustrated by summarizing a number of findings related to the use of psychotropic drugs with schizophrenic patients. The need for further longitudinal investigations of the effects of the durgs on gonadotropin excretion and sperm production is therefore apparent. In view of the limited data, caution is urged in the use of large doses with preadolescent males, since they could potentially alter or modify the sequence and balance of endocrine mechanisms essential to normal puberty. 58 references.

100531 Shader, Richard I.; Nahum, Jeremy P.; DiMascio, Alberto. Psychiatry Department, Massachusetts Mental Health Center, Harvard Medical School, Boston Amenorrhea. ***In: Shader, R., Psychotropic drug side effects.*** **Baltimore, Williams & Wilkins, 1970, 290p.(p.10-15).**

In a discussion of the effects of psychotropic drugs on endocrine and metabolic functions, the nature and treatment of amenorrhea and other menstrual irregularities are examined. Clinical reports dealing with amenorrhea induced by psychotropic drugs have suggested a variety of theories and findings. Treatment with chlorpromazine, thioridazine, and other tranquilizers was particularly significant in the incidence of amenorrhea, but any simple formulation of the mechanisms involved was compromised by the finding that these compounds are also effective in the therapy of so-called functional amenorrhea. In psychotic patients, the condition has been associated with increased, decreased, and normal urinary gonadotropin levels. Although the appearance of amenorrhea should not cause alarm, it should alert the physician to conduct an adequate medical evaluation to rule out pregnancy and other organic causes. Before placing female patients of childbearing age on such a regimen, a careful menstrual history should also be taken. Several case histories are reviewed to illustrate the development of amenorrhea associated with the use of psychotropic drugs. 21 references.

100533 Shader, Richard I. Psychiatry Department, Massachusetts Mental Health Center, Harvard Medical School, Boston, Massachusetts Ejaculation disorders. ***In: Shader, R., Psychotropic drug side effects.*** **Baltimore, Williams & Wilkins, 1970. 290p.(p.72-76).**

In a discussion of the effects of psychotropic drugs on male sexual function, the incidence of ejaculation disorders is examined. The occurrence of aspermia, or the absence of ejaculation during coitus or masturbation, is often noted with thioridazine. Although this condition has not been reported with other phenothiazines, single case studies describe ejaculation disorders associated with other psychotropic drugs. Possible causal factors are suggested, including action of the drug as an adrenergic blocking agent. The condition does not appear to be dose related, and return of function will occur with discontinuance of the offending drug. Other drugs are usually substitutable in order to maintain the desired therapeutic effect without causing aspermia. 20 references.

100534 Shader, Richard I.; Belfer, Myron L.; DiMascio, Alberto. Psychiatry Department, Massachusetts Mental Health Center, Harvard Medical School, Boston Thyroid function. ***In: Shader, R., Psychotropic drug side effects.*** **Baltimore, Williams & Wilkins, 1970.290p.(p.25-45).**

In a discussion of the effects of psychotropic drugs on human endocrine and metabolic function, the action on thyroid metabolism is examined. Some of the literature on thyroid metabolism in mental illness is reviewed, as well as the controversial and sparse material on the effects of the more commonly prescribed psychotropic drugs on thyroid metabolism. Psychological factors related to the development of hyperthyroidism are treated, along with the many documented reports of the effects of traumatic stress on thyroid function in general. Findings indicate that it is unwise to apply specific results from animal studies to the changes in thyroid activity during stress in man. Possible causes for the contradicting data are suggested, as well as a number of theories involving the mechanism of action and the influence of neurological factors. It is concluded that documented cases of thyroid disease resulting from the use of these drugs are not sufficient to warrant definite decision, but their administration in patients who are hypothyroid or hyperthyroid must be undertaken with caution. In addition, the causal relationship between emotion and thyroid illness and psychosis and thyroid function are not proven, although the data in the former situation are quite suggestive. The question of the mediating

mechanisms in the interaction between psychological stress and observed changes in thyroid function remains unanswered and represents a potential field for the investigative use of psychotropic drugs. 112 references.

100997 Heinrich, K. Universitats-Nervenklinik Mainz, Mainz, Germany /Etiology of late hyperkinesis in the course of long-term treatment with neuroleptics./ Zur Atiologie spater Hyperkinesen im Verlaufe der neuroleptischen Langzeittherapie. *Psihofarmakologija 2: Radovi Drugog Jugosl.Psihof.Simpozija -- 1969.* Zagreb, Medicenska Naklada, 1970.441 p. (p.187-193).

Extrapyramidal side-effects of prolonged neuroleptic therapy are described, with particular emphasis on the late developing hyperkineses. An analysis of such effects following neuroleptic treatment in 755 patients is presented, with was based on a questionnaire. Results revealed that 12.3% of the male (354) and 20.2% of the female (401) patients showed late, extrapyramidal hyperkineses, predominantly in the tongue movement disorders and those of the facial musculature.

101020 Gross, H.; Kaltenback, E. Neurohistologisches Laboratorium, Psychiatrisches Krankenhaus der Stadt Wien, Baumgartnerhohe, Vienna /Neuropathology of persistent choreiform hyperkinesias under long-term treatment with neuroleptics./ Zur Neuropathologie der persistierenden choreiformen Hyperkinesen unter neuroleptischer Langzeittherapie. *Psihofarmakologija 2: Radovi drugog Jugosl.Psihof.Simpozija -- 1969.* Zagreb, Medicenska Naklada, 1970.441 p. (p.195-204).

From investigations in progress on persistent hyperkinesis, it is claimed that not more than 2% of neuroleptic treated patients are thus affected. The reason for this low figure (compared to reports in the literature) is presumed to be due to the administration of lower doses, and the withholding of this type of therapy from patients with known brain damage, particularly from arteriosclerotics. Some of the findings include brain changes following long-term therapy regardless of hyperkinesis, which are characterized by a satellitosis and a neuronophagia of the large cell elements, as well as by a gliose mesenchymal reaction in the nucleus caudatus. Changes in the direction of neuroaxonal dystrophy in the area of the substantia nigra are probably related to the neuroleptic Parkinson Syndrome, but may also be caused by chronic alcoholism. In most cases of diagnostic error, the persistent hyperkinesias were mistaken for choreiform symptoms, and thorough clinical investigation of the causes is urged. 14 references. (Author abstract modified)

105560 DiMascio, Alberto; Shader, Richard I.; Harmatz, Jerold S. Psychiatry Dept., Tufts Medical School, Mass. Behavioral toxicity. Part 5: gross behavior patterns. *In: Shader, R., Psychotropic drug side effects.* Baltimore, Williams & Wilkins, 1970. 290 p.(p.142-148).

The behavioral toxic effects of psychotropic drugs are discussed as they relate to inducement of acute psychotic reactions. Such gross behavior patterns include both paradoxical effects, or those alterations in mood in a direction opposite to the clinically desirable one, and pendular effects, or those alterations that proceed in the desired direction to the degree that the resultant mood tends toward the opposite state for which the drug was initially administered. Complete mental and personality disorientation and extremely violent or excited behavior have been noted as a result of these drugs. Some question exists over whether or not these phenomena are merely the uncovering of latent schizophrenic symptoms. Although such extreme reactions are not widely reported in the literature, the disastrous consequences, both therapeutically and to the potential health of the patient, are such that they demand increased awareness of the phenomena and more intensive investigation aimed at explaining these reactions if they are to be avoided. 48 references.

106769 Shopsin, B.; Johnson, G.; Gershon, S. Neuropsychopharmacology Research Unit, Department of Psychiatry, New York University Medical Center, 550 First Avenue, New York, N.Y. 10016 Neurotoxicity with lithium: differential drug responsiveness. *International Pharmacopsychiatry (Basel).* 5(2-4):170-182, 1970.

Testifying to lithium's apparent specificity in mania, a double-blind controlled evaluation of lithium and chlorpromazine indicated that 85% of schizo affective patients treated with lithium carbonate showed an overall worsening of their clinical status. A significant feature of this group was the appearance of symptoms of organicity such as disorientation, confusion and reduced comprehension. Along with this change there was an increase in the severity of the basic psychopathology; the thought disturbance often became more

pronounced with psychomotor excitation, delusional thought and hallucinations. The occurrence of these apparent toxic effects was at blood levels between 1.16 and 1.97 mEq/l, levels not usually associated with toxic phenomena in manic individuals. A later investigation allowed for the possibility of experimental design as accounting for toxicity and poor response in schizophrenic subjects. A follow up study was carried out, where lithium or chlorpromazine was issued to schizophrenic patients under conditions where lithium medication was carefully monitored in efforts to avoid toxicity. Previous findings confirmed neurotoxic symptoms in 6 of the 11 schizophrenic subjects given lithium. Observed neurotoxic changes on modest lithium dosage and blood levels in a cyclic manic-depressive interphase, and a patient manifesting an acute depression episode are reported. Eight case reports deal comprehensively with various neurotoxic changes appearing during treatment with lithium carbonate, under-scoring the apparent disease specific therapeutic effect of lithium and focusing on the findings of decreased threshold tolerance to lithium in schizophrenic patients. 46 references.

113137 Cordeiro, Marco Antonio P. R.Leopoldo Miguez 129, Copacabana Z.C.07, Rio de Janeiro, Brazil /Suicide and paranoid defense (preliminary report)./ Suicidios e defesa paranoide (nota previa). *Revista de Psiquiatria (Rio de Janeiro).* 10(18):29-33, 1970.

The cases of four paranoid patients are presented in whom long lasting treatment with unspecified doses of strong neuroleptics, such as butyrophenones and sustained release fluphenazine, produced clinical improvement, but the patients tried to commit suicide while under ambulatory therapy. The results suggest that the use of strong neuroleptics produces depression which deprives the patient of his paranoid defense and leads to self-destruction. 12 references.

121795 Veitzman, V. no address /Applied clinical psychopharmacology./ Psico-farmacologia clinica aplicada. Buenos-Aires, Lopez Libreros, 1970, 294 p.

Indications, contraindications, nosology, toxicity, mode of administration, and incompatibilities of different large groups of drugs used in psychopharmacology are methodically studied. Each compound is examined in turn, with the role of the placebo being discussed afterwards. At the end of the work, the author proposes several treatment programs to be used in the course of various syndromes and gives a list of substances included in the drug groups recognized and authorized in the Argentine Republic. A substantial alphabetical index completes a work which should be useful to numerous clinicians.

124311 Bertolotti, P.; De Pietri, L. Istituto Psichiatrico 'S.Lazzaro', Reggio Emilia, Italy /Psychosensorial phenomena during treatment with tricyclic thymoanaleptics (presentation of two cases). Fenomeni psicosensoriali in corso di trattamento con timoanalettici triciclici (segnalazione di due case). *Riv.Sper.di Fren.e Med.Legale delle Alienazione Ment. (Reggio Emilia).* 94(6):1556-1566, 1970.

In a 63 year old woman with depression and a history of hypertension, 15 day treatment with desipramine in daily doses of 75-150mg resulted in disappearance of depression and the parallel appearance of cyclothymia and psychosensorial phenomena which ceased upon treatment with vasodilators and axiolytic and hypnotic agents. In a 54 year old male with melancholia, anxiety and a history of myocardial infarction, daily administration of amitriptyline in doses of 50-75mg for five days resulted in improvement of mood, but he developed hallucinations. When the dose was increased to 125mg daily, the severity of hallucinations increased, administration of mortriptyline was ceased and the patient was placed on clopenthixol. The psychosensorial phenomena disappeared but there was resumption of depression. Subsequent treatment with niamid in daily doses of 100mg for several months improved depression and did not induce psychosensorial disorders. 14 references.

126639 Taylor, W.J.Russell. Clinical Pharmacology-Toxicology Ctr., Philadelphia General Hospital, Philadelphia, Pa. 19104 A comparative determination of side effects associated with the oral use of three anticholinergic-psychotropic drugs. *Int.Z.fur klinische Pharmakologie, Therapie und Toxikologie (Munchen).* 3(1):1-13, 1970.

A 6 week clinical trial was carried out in 181 volunteers from the Philadelphia and Newark areas on the anticholinergic drugs Pamine-Pb, Librax and Pro-Banthine-Pb, in order to compare their side effects. Incidence and severity of side effects was greater with Pamine than with the

other 2 drugs, and more Ss felt it necessary to discontinue Pamine medication. Librax caused the least number of dry mouths. Pamine caused the most severe constipation. Expected rise in heart rate was highest with Librax. With all 3 drugs, females showed higher heart rates and greater tendency to experience constipation; males suffered more from difficulty with micturition. In general, all test combinations were tolerated well. Headaches were markedly reduced when compared with placebo. 4 references. (Author abstract modified)

128389 Speiser, P.; Kern, R.; Kloti, R. Universitats-Augenklinik, Ramistr. 100, CH-8006 Zurich, Switzerland /Drug-induced damage of the eye and the optical nerve./ Medikamentose Schadigungen des Auges und des Sehnervs. *Therapeutische Umschau (Bern).* 27(6):394-399, 1970.

Damage to the eye and the optic nerve caused by drugs has a variable prognosis. These drugs may alter some of the visual functions or lead to morphological changes in the different parts of the eye. Such modifications may be reversible or irreversible. Every form of complaint involving the eye, whether observed by the patient or the physician, should be taken seriously and referred to an ophthalmologist. Experience has shown that apart from individual sensitivity to certain toxic allergic reactions, treatment with high doses of psychopharmacological agents, quinoline derivatives and steroids, used over extended periods, may cause most serious damage to the eye. 8 references. (Author abstract modified)

128390 Angst, J. Psychiatrische Universitatsklinik, Lenggstr. 31, CH-8008 Zurich, Switzerland /Psychopharmaceuticals and neurological side effects./ Psychopharmaka und neurologische Nebenwirkungen. *Therapeutische Umschau (Bern).* 27(6):356-360, 1970.

Neurological side-effects in psychopharmacotherapy are discussed. Initially and during the first months of treatment the most pronounced symptoms consist of tremor, paroxysmal dyskinesias, akathisia and Parkinsonism. Paroxysmal dyskinesias are frequently mistaken for hysterical symtoms and are not specifically treated. Akathisia is frequently overlooked. The diagnosis of late extrapyramidal hyperkinesis as a complication of prolonged neuroleptic treatment is particularly important. Such disturbances may persist even after discontinuation of the drug and may be irreversible. Early diagnosis and careful adjustment of dosage aid in the prevention of chronic defects attributable to psychopharmaceuticals. Predisposing factors in the occurrence of various neurological side-effects are discussed. 15 references. (Author abstract modified)

129753 Mitsuyama, Yoshio; Yukitake, Akira. Department of Neurology, Omuta Rosai Hospital, Japan Two cases of acute para-chlornitrobenzene poisoning sequelae. *Clinical Psychiatry (Tokyo).* 12(5):413-420, 1970.

Two cases of acute chlornitrobenzene poisoning sequelae are reported. Para-chlornitrobenzene (pCNB) is one of the derivatives of benzene which dissolves in alcohol and ether, and by high heat. The maximum permissible intake amount is considered to be 1ppm. One patient was a 36-year-old male who worked packing pCNB in bags for 12 years and did not show any toxic symptoms except occasional stomach and intestine disorder. At the time of the onset of the toxic symptoms, his blood pressure was 120/80mmHg, his pulse rate was 100/min, and his body temperature was 36.0degrees C. Another patient was a 53-year-old male who worked in a dye industry for five years, and had been hospitalized for heavy drinking at one time. He worked packing pCNB for seven hours one day and had toxic symptoms on the same day after drinking. He fell into a trance after two hours of the onset of the symptoms, and his blood pressure was 160/80mmHg with no abnormality in the pulse and heartbeat. Topics discussed are: progress from the onset to the time of sequelae; symptoms during the sequelae such as articulatory disorder, walking disturbance, abnormal tension of limb muscles, and reflex abnormality; toxic symptoms such as intellectual disorder, emotional disorder, change of personality, skin reaction; and the cause of the sequelae such as the delay in treatment during the acute period and drinking before the onset of symptoms. 11 references.

16 METHODS DEVELOPMENT

102119 Shapiro, I.L.; Grinberg, K.N.; Zhurkov, V.S.; Torba, V.A. Moscow, USSR /On the mutagenic effect of medicinal preparations used in psychiatry. (Review of the literature.)/ O mutagennom effekte lekarstvennykh preparatov, primeniaemykh v psikhiatrii. (Obzor literatury.) *In: Efroimson, V., Genetika psikhicheskikh boleznei.* Moscow,

Min.Zdravookhraneniia RSFSR, 1970. 316 p.(p.85-102), v.60.

Review of studies on the mutagenic effect of pharmacological preparations indicates great divergence of opinion due to experimental difficulties encountered in the wide variety of test objects and the inaccessibility of investigation of mutagenic effects in human sex cells. Objects used in testing were bacteria, drosophila, mice, primary cultures of human cells, and human lymphocytes which received varying dosages of pharmacological drugs. Both genetic and cytogenic methods for calculating mutagenic activity can be applied to mice and drosophila, but cytogenic methods are used almost exclusively for investigation in humans. Thus, extrapolation of data on the frequency of chromosomal mutation in somatic cells to the frequency of genic mutation in sex cells can be achieved only on the basis of very approximate calculations. Since no single test object or method employed yields precise, verified information that is applicable to the human with minimal extrapolation, trials for mutagenesis should be conducted on a battery of test objects with methods that have been maximally standardized according to techniques of administration and calculation. 45 references.

112282 Chistoni, G.C.; de de Perrot, E.; Niederberger, W. Policlinique psychiatrique universitaire de Lausanne, CH-1000 Lausanne, Switzerland /Research in new experimental methods for psychotropic drugs: results of a double-blind study with a new tranquilizer, Nobrium./ A la recherche de nouvelles methodes d'experimentation des medicaments psychotropes: resultats de l'essai en double aveugle d'un nouveau tranquillisant, le Nobrium. ***International Pharmacopsychiatry (Basel).***

A clinical study was undertaken with an anxiolytic drug using a new approach, both as regards the method of testing and the evaluation of results. In the first phase of the study a series of 109 patients was given the anxiolytic Nobrium and in the second phase a further series of 87 patients was given a placebo. The administering physicians were not told of the substitution of placebo for Nobrium in the second series. Investigations were performed to determine whether the tablets were taken regularly. On completion of treatment a statistical analysis was carried out to compare various parameters, such as incidence of side effects, influence of age, effect on target symptoms, in the 2 groups of patients. The results demonstrated clearly the considerable anxiolytic properties of the active drug, showing its effect on sleep disturbances and anxiety to be significantly greater than its effects on the other target symptoms studied and the effects of placebo. 12 references. (Author abstract modified)

17 MISCELLANEOUS

104836 Ponti, Gianluigi. Facolta di Medicina, Universita di Milano, Milan, Italy /Psychopharmacological agents in the treatment of the criminal./ Gli psicofarmaci nel trattamento della criminalita. *Quaderni di Criminologia Clinica (Rome).* 12(2):205-236, 1970.

The use of drugs in the treatment of the criminal is reviewed. While the treatment of the psychopathic criminal is the concern of psychiatry, the use of psychopharmacological agents seems adequate for the treatment of criminals with subpsychotic conditions, behavior disorders, neurotic epileptic and involutional disturbances. Although drugs alone cannot cure the criminal, further research in this area is needed. 61 references.

105266 Isbell, H.; Chrusciel, T.L. Department of Medicine, University of Kentucky Medical Center, Lexington, Kentucky Hallucinogens. *In: Isbell, H., Dependence liability of 'non-narcotic' drugs.* Geneva, WHO, 1970. 111 p.(p.80-99).V.43 (Supplement).

Technical information is presented on psychoactive drugs considered to have an actual or potential capacity to produce central nervous system hallucination. The general group is described with particular focus on specific types, including indoles, phenylalkylamines with methoxy-substituents on the phenyl ring, hallucinogenic anticholinergics, tetrahydrocannabinols, and miscellaneous hallucinogens. Tables include data on chemical description, names, symptoms of intoxication, tolerance, psychic dependence, pharmacological notes, major dangers of abuse, and abuse potential rating. 96 references.

105336 The Council of State Governments. The Council of State Governments, Iron Works Pike, Lexington, Kentucky 40505 State drug abuse contorl. Lexington, Kentucky, Council of State Governments, 1970. 45 p. $3.00.

The overall picture of drug abuse is reviewed and discussed. Drugs can mean any substance capable of altering psychic or behavioral activity, and the use of some of them, such as medicines and alcohol, is acceptable to society. Defining acceptable uses is a continuing social issue. For those drugs determined to be socially undesirable or harmful, the states must develop or maintain a program to alleviate the problems generated by usage: law enforcement to apprehend and punish users and distributors, treatment of addicts, and education of potential users to curb the spread of drug use. There are 3 major sections, the drug abuse problem, federal responses to drug abuse, and narcotics activities in the states. 13 references. (Author abstract modified)

105734 Fokstuen, T. Sigfrids sjukhus, Vaxjo, Sweden Clinical trials and treatment with psychopharmaceuticals. A second critical review: an impression. *International Pharmacopsychiatry (Basel).* 5(1):2-15, 1970.

Some impressions are offered concerning clinical trials and treatment with psychopharmaceuticals. Attention is called to psychiatric observations which everybody can make, which may not be very scientific but nevertheless are actual facts of importance to the patient and therefore should be taken seriously. These facts are of great concern to psychiatry and to the system of reference since this system should be based on, or include, any changes in the patients even when these are in matters which are considered unimportant. Discussion is primarily concerned with how patients undergoing treatment and participating in clinical trials experience this, together with the difference between their experience and the ideas held by those who have professional dealings with them. (Author abstract modified)

106770 Lopez Ibor Alino, J.J.; Lopez Ibor Alino, J.M. Clinica Lopez Ibor, 78, av.Nueva Zelanda, Puerto de Hierro, Madrid 35, Spain Indications of lithium salts in psychosomatic medicine. *International Pharmacopsychiatry (Basel).* 5(2-4):187-189, 1970.

The lithium salts have demonstrated their efficacy in the treatment of several types of affective disorders, such as manic states and the prevention of recurrent phases. Some new indications of lithium salts in psychosomatic medicine are discussed, with particular reference to the use of lithium in depressive equivalents and the phenonenon of the syndrome shift. 6 references. (Journal abstract modified)

106782 Freyhan, F.A. author address not given Lithium: some critical considerations. *International Pharmacopsychiatry (Basel).* 5(2-4):77-79, 1970.

Lithium treatment has increased diagnosis of affective disorders, brought new insights into the biochemical and physiological correlates of mood variation and mood disorders, contributed to distinctions between unipolar and bipolar manifestations of affective disorders, and presented new theoretical problems regarding long-term evaluations of natural versus drug modified periodicity of affective disorders. One major advantage of lithium is the need for determining serum levels to monitor lithium intake. Long-term treatment of schizophrenic patients with neuroleptic compounds paved the way for community psychiatry which has maintained as its major objective the transition from hospital to nonhospital care. Recent evidence suggests that long acting neuroleptics may be as effective in preventing rehospitalization of schizophrenic patients as lithium is reported to be in reducing hospitalization rates of affectively ill patients. 2 references.

108212 Liu, Chun Yeh. author address not given Drugs and mental control. *The Intellectual (Taipei).* 33:10-13, 1970.

The use of drugs as tools to control the mind or to heighten freedom of the mind is discussed. The results of clinical research and controlled experiments with tranquilizers, sedatives, stimulants, antidepressive drugs, and psychotomimetic drugs are reported. Special attention is paid to the ability of certain drugs to alter or enhance creativity, imagination, and mood. While a certain amount of progress has been made in controlling mental illness with drugs, the problems involved in attempting to use drugs to expand human mental capacity seem at present to be insurmountable. Virtually all experimentation to date in this latter category has been biased by the use of subjects who are either mentally ill or who are so enthusiastic about the research that results are unreliable.

110105 Borts, M.I.; Vovina, E.N.; Kogan, S.I. Leningrad, USSR /On the question of the prophylaxis of initial manifestations of presenile psychoses./ K voprosu profilaktike nachal'nykh proiavlenii presenil'nykh psikhozov. *In: Efimovich, N., Klin., patogenez i lechenie nervno-psikh.zabolevanii.* Moscow, Sovet Ministrov RSFSR, 1970. 335 p.(p.98-102).

Successful experiments with the treatment of reactive conditions in the presenile period in an outpatient clinic justify outpatient treatment as an important means of prophylaxis in presenile psychoses. Against a background of obligatory psychotherapy, tranquilizers, antidepressants, small dosages of insulin, and injections of aloe and magnesium and glucose solutions were administered. In the absence of contraindications, work therapy was prescribed.

110225 Isbell, H.; Chrusciel, T.L. Department of Medicine, University of Kentucky Medical Center, Lexington, Kentucky Central nervous system depressants. *In: Isbell, H., Dependence liability of 'non-narcotic' drugs.* Geneva, WHO, 1970. 111 p.(p.10-62).v.43 (Supplement).

Technical information is presented on psychoactive drugs considered to have an actual or potential capacity to produce central nervous system depression. The drugs are those that relieve anxiety (sedatives) or induce sleep (hypnotics). Detailed discussion is presented with tabular data for: barbiturates or diureides, monoureides, halogens, chloral and derivatives, tertiary acetylenic alcohols, cyclic ethers, carbamic acid esters of monohydroxy alcohols and of glycols, piperidinedione derivatives, quinazolinones, benzodiazepines, sulfonmethanes, and miscellaneous agents. Tables include data on chemical description, name, symptoms of intoxication, tolerance, psychic dependence, pharmacological notes, major dangers of abuse, and abuse potential rating. 151 references.

110226 Isbell, H.; Chrusciel, T.L. Department of Medicine, University of Kentucky Medical Center, Lexington, Kentucky Central nervous system stimulants. *In: Isbell, H., Dependence liability of 'non-narcotic' drugs.* Geneva, WHO, 1970. 111 p.(p.63-79).v.43 (Supplement).

Technical information is presented on psychoactive drugs considered to have an actual or potential capacity to produce central nervous system stimulation. The general group is described along with specific types, including: ephedrine and derivatives, amphetamines, piperidine derivatives, and miscellaneous agents. Tables include data on chemical description, names, symptoms of intoxication, tolerance, psychic dependence, pharmacological notes, major dangers of abuse, and abuse potential rating. 80 references.

110897 Porter, R.; O'Connor, M. author address not given Molecular properties of drug receptors. London, Churchill, 1970. 298 p.L4.00.

The theory of drug receptors has long fascinated pharmacologists as a potential bridge between drug action and chemical structure. A Ciba Foundation symposium volume indicates the interest which receptors are now attracting among molecular biologists and protein chemists.

111254 Portnova, I.A. Dmitrovskaya psikhiatricheskaya bol'nitsa No.9, Dmitrov, USSR /Some problems of organizing the psychotherapeutic environment in a mixed female psychiatric ward./ O nekotorykh voprosakh organizatsii psikhoterapevticheskoy sredy v smeshannom zhenskom psikhiatricheskom otdelenii. *In: Shternberg, E., Problemy organizatsii psikhiatri.pomoshchi kliniki.* Moscow, Sovetskaya Rossiya, 1970. 103 p.(p.84-87), Part 2.

The problems of organizing effective methods of treating mental illnesses, especially when psychopharmacological agents are used, and the interrelationships between female patients and medical personnel are discussed. In a mixed ward, patients who are being administered neuroleptic agents assist the medical personnel and nurses in care of other patients and of themselves. Organization of a therapeutic environment in the mixed psychiatric ward created a completely new attitude of the patient toward the hospital and toward his stay in the hospital. The regimen of the ward itself becomes therapeutic in the true sense of the word, contributing to prevention and treatment of psychotic states. The system of mutual respect and a concerned attitude of the patients and medical personnel towards each other reduces the number of extreme occurrences. Finally, conditions are created for improving the quality of remissions in both the medical and social aspect.

111933 Osmond, Humphrey; Aaronson, Bernard. author address not given Psychedelics: the uses and implications of hallucogenic drugs. Garden City, N.Y., Anchor-Doubleday, 1970. 512 p.$2.45.

A series of papers designed to provide an understanding of psychedelic drug use from a particular frame of reference is presented. Included are sections on: the feelings as well as the observable detail of a drug experience; the anthropologic and religious considerations of tripping; the psychedelic effects on mental function; therapeutic applications of psychedelic drugs; group therapy; nondrug analogues to the psychedelic state; hypnotic analogues; sociologically oriented comments on the drug scene; and comments on the press which the whole drug question has received.

115114 Korolkovas, Andrejus. no address Essentials of molecular pharmacology: background for drug design. New York, Wiley-Interscience, 1970. 340 p. $16.50.

Fundamental principles of drug actions at the molecular level are illustrated in terms of modern chemistry and biochemistry. Consideration is given to physiochemical properties of small molecules, pharmacological effects of specific moieties and an analysis of drug receptor interactions. Receptor topography is discussed, and theories and mechanisms of drug action are appraised.

115463 Wittenborn, J.R.; Goldberg, Solomon C.; May, Philip, R.A. Department of Psychology, Rutgers University, New Brunswick, NJ Psychopharmacology and the individual patient. New York, Raven Press, 1970.256 p.$12.95.

The development or application of methodologies for predicting the outcome of treatment with psychotropic medications are presented by 41 contributors. Topics include: problems in predicting outcome in various populations (the schizophrenias, depressions, outpatients, and geriatrics), utilizing laboratory responses to acute drug dosages to estimate longer term clinical improvement, and selecting demographic, personality, and biological predictors of response to different drugs.

119840 Calne, Donald B. author address not given Parkinsonism: physiology, pharmacology and treatment. London, Edward Arnold, 1970. 148 p. L2.25.

The physiology, pharmacology and treatment of parkinsonism is reported. To make effective use of L-dopa in the treatment of the disease the mechanisms of the main symptoms of the syndrome are discussed. These aspects include: motor control, hypokinesia, the pharmacology of L-dopa, dopaminergic transmission and a survey of treatment. Treatment and disease type omissions are noted.

119884 Knopp, W. Ohio State University, College of Medicine, Dept. of Psychiatry, Columbus, Ohio Man's tripartite brain and psychosomatic medicine. *Psychotherapy and Psychosomatics (Basel).* 18(1-6):130-136, 1970.

Graphically documented clinical observations and quantitative evaluations are reported of 2 lon-

gitudinal studies involving 1 case of Tourette's Disease and 25 acute schizophrenics treated by high potency neuroleptics. The findings indicate that symptoms expressing dysfunction of the dopaminergic nigrostriatal system seem to be drug and dosage related, while those expressing dysfunction of hypothalamic integration (noradrenergic) seem to be related to factors other than neuroleptic drugs. Supporting evidence is cited from the literature pointing out a possible existence of at least 2 levels of 'central' integration. It is assumed that a functional dysharmony or a split between such levels may be cause, effect or concommittant of psychosomatic disease. 12 references. (Author abstract)

121080 Marrazzi, A. S. University of Missouri Institute of Psychiatry, St. Louis, MO A neuropharmacologically based concept of hallucination and its clinical application. *In: Keup, W., Origin and mechanisms of hallucinations.* New York, Plenum Press, 1970. 479 p. (p. 211-225).

A neuropharmacologically based concept of hallucination is presented along with its clinical application. It is suggested that hallucination may afford a key to the understanding of function in the experimentally and clinically disturbed nervous system, and it is shown, by recording the signals arriving at the various areas of the cerebral cortex, that hallucinogens reduce and finally interrupt access to association areas as part of an action, which in larger doses disconnects other parts of the brain as well. The diagnostic potentiality and the utility in monitoring the course of an illness are illustrated, using a simple test procedure requiring no verbal communication after the initial period of familiarization. 11 references.

122098 Barbeau, A.; McDowell, F.H. no address L-dopa and parkinsonism. Davis, Philadelphia, 1970. 124 p. $12.00.

The proceedings of a conference on L-dopa and Parkinson's disease, held in November of 1969 in Val David, Quebec, are presented. The material includes a series of generally brief communications from a large number of workers, as well as verbatim general discussion. In addition, there is a summary of the conference which gives an historical background of the problem. The book itself accepts the status of L-dopa in the treatment of Parkinson's disease and considers the problems which still exist along with future prospects in the field. The main questions which remain unanswered deal with the reasons why L-dopa does not have a beneficial effect on some people, the mechanism for the effect of the drug, the underlying mechanism for the side-effects of the drug, and the possibility of finding a form of therapy which will prove better than L-dopa.

122378 Lapin, I.P. Leningradskiy nauchno-issledovatel'skiy psikhonevrologicheskiy institut imeni V.M.Bekhtereva, Leningrad /Depressive states as a pharmacological target./ Depressivnyye sostoyaniya kak ob'yekt farmakologicheskogo vozdeystviya. *In: Farmakologicheskiye osnovy antidepressivnogo effekta.* Leningrad, Ministerstvo Zdravookhraneniya RSFSR, 1970. 165 p. (p.13-17).

A scheme of basic biochemical disorders occurring in patients with endogenous depression is suggested as a guideline for biochemical pharmacological studies required for the development of new antidepressant drugs. It includes decreased brain serotonin and noradrenaline levels, decreased blood tryptophan and tyrosine levels (serotonin and noradrenaline precursors, respectively) and lowered 5-oxyindolylacetic acid and vanillylmandelic acid levels in the cerebrospinal fluid. Increased urinary kynurenine levels, reflecting enhanced liver tryptophan pyrrolase activity, and higher blood and urinary corticosteroid levels correlate with the extent of tension and depression states. The depressive state is attributed to the inhibition of serotoninergic processes while activation of the mandelic acid system is thought to cause the anxiety and tension symptoms. Involvement of serotonin in the pathogenesis of depression indicates the need for new drug testing in terms of their serotoninergic activity as opposed to the traditional screening tests which focus only on the adrenalin stimulating action. Inhibition of the hypothalamus involved in depression suggests the possibility of antidepressant treatment combined with weak tranquilizing features. The role of kynurenine and its metabolites in the pathogenesis of endogenous depression is still unknown.

124312 Frick, Bruno. Istituto de Ergoterapia Psichiatrica, Stadio-Ora, Italy /Experiences of a therapeutic community./ Esperienze da una comunita terapeutica. *Riv.Sper.di Fren.e Med.Legale delle Alienzione Ment. (Reggio Emilia).* 94(6):1547-1555, 1970.

In addition to the rehabilitation activities, 97% of the psychiatric patients at the Stadio-Ora In-

stitute of Occupational Therapy, in Italy, were also treated with chemotherapy, including fluphenazine decanoate administered intramuscularly in single monthly doses of 12.5-75mg for patients who refused oral treatment. No specific details are given but it is mentioned that the use of symptomatic drugs such as hypnotics and transquilizers was avoided and that treatment consisted mainly of psychotropic, anticonvulsants as well as drugs used for the therapy of Parkinson's disease. Furthermore, the activities of the therapeutical community were organized democratically according to a liberal schedule established by the patients themselves. The results obtained are satisfactory. Many patients with long histories of psychiatric diseases were discharged and others are given passes to spend time with their families or employed meaningfully. 15 references.

124320 De Fazio, F.; Buondonno, E. Cattedra di Antropologia Criminale, Universita di Modena, Modena, Italy /Thioridazine and behavior disorders (perspectives for the use of the drug in criminology)./ Tioridazina e turbe comportamentali (prospettive di utilizzazione del farmaco in campo criminologico). *Riv.Sper.di Fren.e Med.Legale delle Alienazione Ment. (Reggio Emilia).* 94(6):1496-1504, 1970.

A review of the literature relavant to the use of thioridazine in psychiatry is presented which makes special reference to the treatment of behavior disorders and points out significant data concerning drug therapy in prison inmates. Administration of thioridazine for several months to a total of 280 psychiatric patients is analyzed. Finally, possible uses of thioridazine and other drugs in different operating sectors of clinical criminology are suggested.

126778 Kumano, Akio. Tokyo University Medical School, Tokyo, Japan Abstract of theses for doctor of medical sciences, the University of Tokyo: Morita therapeutic approach to schizophrenia. *Tokyo Journal of Medical Sciences (Tokyo).* 78(4):356-357, 1970.

A combination of Morita therapy and psychopharmacological therapy was given to 51 schizophrenics who were hospitalized at Suzuki Sanatorium from 1962 to 1966; the degree of improvement during the therapy and the prognosis after leaving the hospital are studied. The process of Morita therapy consists of periods of absolute bed rest periods of light work, periods of heavy work, and periods of real life training. Nine patients out of 51 dropped out after the period of absolute bed rest, and these patients were identified as hebephrenic, and depersonalized patients. The improvement in the symptoms during the therapy, and the good state of adjustment after leaving the hospital are considered to be highly related to the patient's intention to participate in the therapy, his receptive attitude, and the patient's good understanding of the therapy. Intelligence, an introspective attitude and strong will are necessary on the part of schizophrenic patients as well as patients with neurosis in order to make the best of Morita therapy.

128509 Barbieri, N. F.; De Caro, E.; Puca, F. M. Clinica delle malattie nervose e mentali dell'Universita di Messina, Messina, Italy /Use of Cattel's I.P.A.T. anxiety scale in a group of neurotic patients before and after psychopharmacological drug and electric shock therapy./ Sull'impiego della scala di ansieta I.P.A.T. di Cattel in un gruppo di pazienti nevrotici prima e dopo terapia con psicofarmaci o elettroschock. *Ospedale Psichiatrico (Napoli).* 38(4):469-479, 1970.

Cattel's Instrument for Personality and Ability Testing (IPAT) anxiety scale of 1957 and the personality factors on which it is based are explained. Its administration, before and after psychotropic drug and electric shock tehrapy, to 20 neurotic patients of both sexes, ranging in age from 17 to 66 years, is described and discussed. The scores obtained before and after therapy and their psychological interpretation are presented. It is concluded that the use of a measuring scale for anxiety satisfies certain essential scientific requirements. The IPAT scale, which permits differentiation between manifest and hidden anxiety, appears to be a concise, rapid instrument with good predictability, especially suitable for psychiatric studies on the efficacy of drugs in the modification of anxious behavior, as well as in normal clinical practice. 11 references.

129237 Hozaki, Hideo. Keio University, Tokyo, Japan Sleeping pills and tranquilizer abuse. *Diagnosis and Treatment (Tokyo).* 58(2):246-249, 1970.

A general discussion on sleeping pills and tranquilizer abuse is presented. Chronic sleeping pill addiction is studied and include such side-effects, or withdrawal symptoms, as convulsion and delirium. Sleeping pills and tranquilizers are

discussed which have recently gained publicity, such as ethnamate, methaqualone, meprobamate, and chlordiazepoxide. The treatment of drug abusers with a description of three drug addicts is given. 2 references.

129564 Joyce, Daphne. no address Drugs, brain and behaviour: proceedings of symposium on psychopharmacology in Durham. Durham, England, University of Durham, 1970. 98 p. L1.10.

Interdisciplinary exchanges on the effects of drugs on the brain and on behavior are given. Seven contributions discuss: (1) the magnitude of human use of psychoactive drugs and the lack of knowledge about their properties and mode of action. It is suggested that animal tests have an important role in the development of psychoactive drugs, but extrapolations from animal to man must take into account the uncertainties involved in the assessment of drug effects in humans. (2) A study of heroin users and a limited study of rapid eye movement (REM) sleep in six heroin addicts. (3) Experimental studies of drug tolerance in rats and the distinction between behavioral and pharmacological tolerance. It is suggested that compensatory behavior by the animal to counteract the effects of a drug accounts for behavior tolerance. (4) Implications for psychopharmacology of the theory of neurochemically coded pathways. (5) A recently developed technique of immunosympathectomy, used to investigate the role of catecholamines in behavior. (6) The general hypotheses that a deficit in neural mechanisms for reward and punishment underlies depressive illness, and that therapeutic drugs act on endogenous chemicals in reward and punishment areas of the brain. (7) Studies concerned with amphetamine barbiturate mixtures.

130417 Scala, A. Ospedale psichiatrico provinciale 'L. Bianchi', Naples, Italy /Biological aspects and nosography of the psychoses (critical note)./ Aspetti biologici e nosografia delle psicosi (nota critica). *Ospedale Psichiatrico (Napoli).* 38(4):583-584, 1970.

Recent developments in psychopharmacology have led to reconsideration of Kraepelin's classification of mental illnesses. Researchers should attempt to work back to the pathogenesis of a disease by further clarifying the pathogenetic mechanism of the symptoms, with the goal of preparing a new classification of mental illnesses based on etiology rather than on symptomatology. The contributions of molecular biology should not be ignored. Ey's organodynamic theory is well suited to a more strictly biological and unitary view of the pathogenesis of psychoses. 1 reference.

134057 Wittenborn, J. R.; Goldberg, Solomon C.; May, Philip R. A. no address Psychopharmacology and the individual patient. London, Pitman, 1970. 256 p. L5.50.

Fourteen papers discussing the prediction of response in an individual patient to treatment with a psychoactive drug are presented. Two aspects of the topic are discussed: how best to describe a patient's characteristics as a basis for prediction; and how to assess the patient's progress during drug, or placebo, treatment.

138145 Ahmed, Syed Haroon. Neuropsychiatric Unit, Jinnah Postgraduate Medical Centre, Karachi, Pakistan Drugs and psychiatry. *Journal of the Pakistan Medical Association (Karachi).* 20(10):313-314, 1970.

An editorial discusses the increasing use of drugs in treatment of psychiatric problems and stresses the importance of understanding the limitations of these drugs in dealing with unique and individualized problems of patients. The sphere of investigation lies in heredity, personality, environment, culture and social history. 1 reference.